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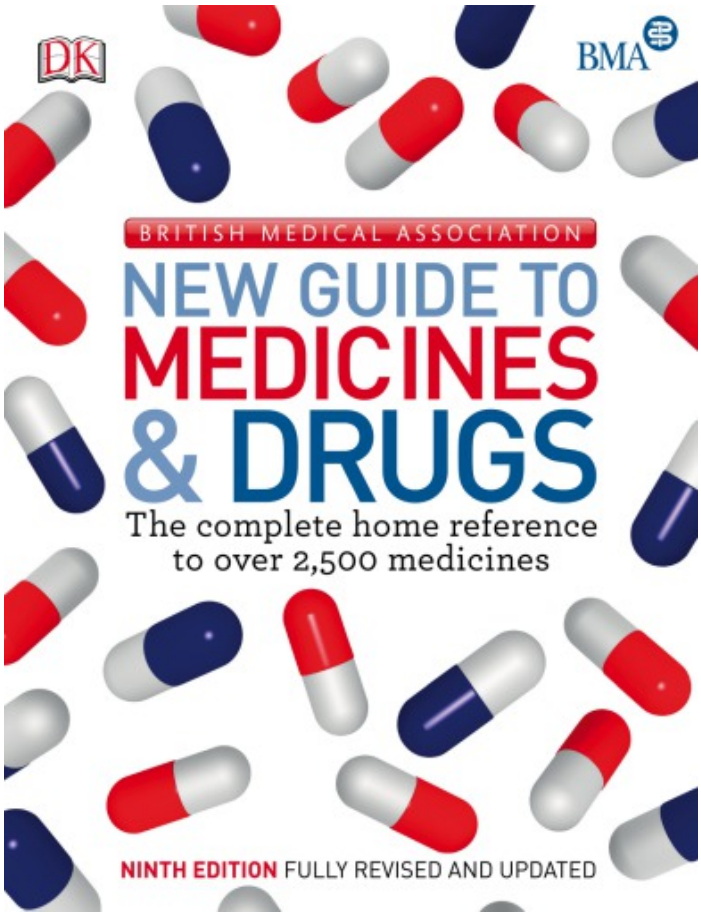

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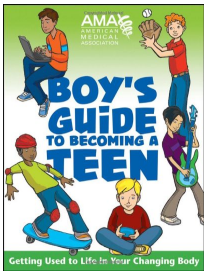

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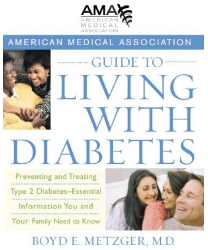
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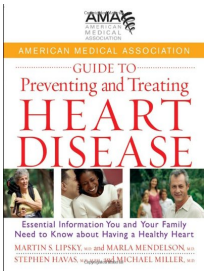
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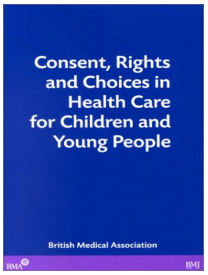

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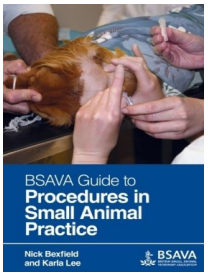

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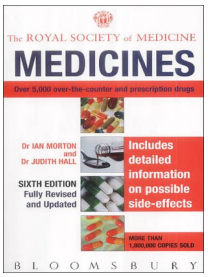

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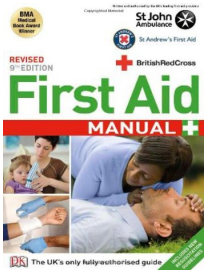

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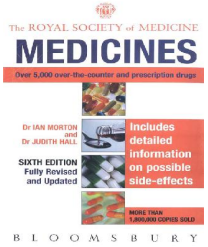

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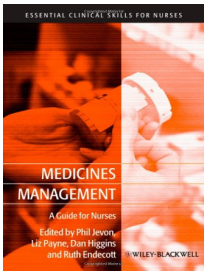

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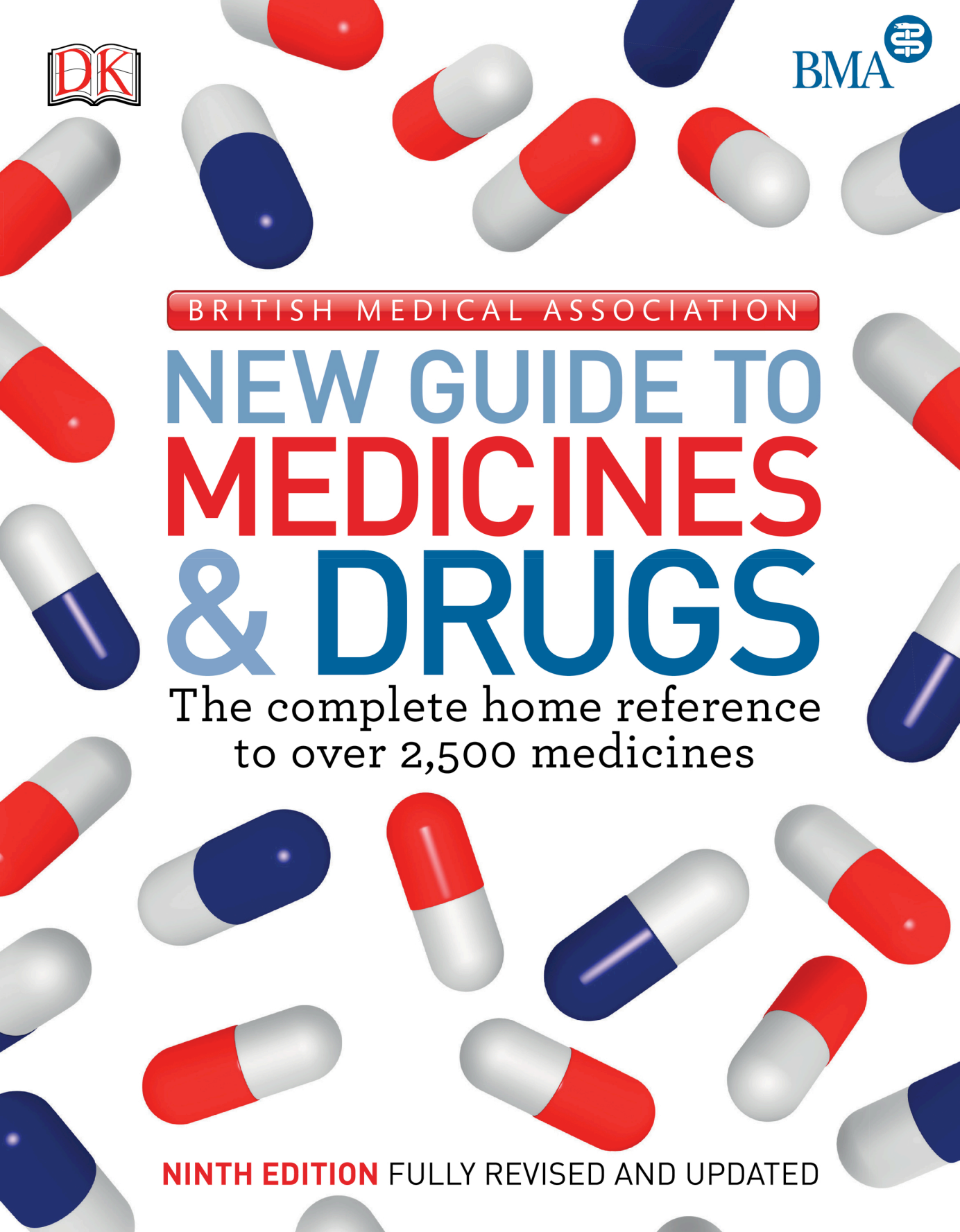
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NEW GUIDE TO MEDICINES & DRUGS
The complete home reference to over 2,500 medicines
NINTH EDITION FULLY REVISED AND UPDATED

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NEW GUIDE TO MEDICINES & DRUGS

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PREFACE

In an age of information overload it is often difficult to know what information is most relevant to you. This is particularly true for medications, as drugs become more sophisticated and manufacturers are required to produce an increasing amount of information detailing side effects, warnings, and interactions with other drugs, including over-the-counter medicines and complementary remedies. There is also a bewildering array of drugs available, and more drugs, previously only available on prescription, can now be purchased over the counter at a pharmacy or supermarket. Moreover, many people also use the internet for information or to buy medications. While some pharmacies operate approved online retail operations, others are not registered or regulated and could supply drugs that are dangerous to your health. For this reason, it is always advisable to consult a health professional before taking any medication, including any complementary remedy. With detailed profiles of 278 drugs, this revised and updated edition of the *BMA New Guide to Medicines and Drugs* guides you through this maze, helping you to prioritise the information that is important in your particular case so that you can use medicines safely and sensibly.

The information in this book has been thoroughly researched and reflects evidence-based medical knowledge. There have been many changes to drug profiles, with revised warnings, dosages, and formulations since the last edition. You can look up an individual drug and easily find the important information you need, for example adverse effects, whether it is safe to take with other medications or in pregnancy, how much to take and when, and whether long-term use causes any problems. It will also inform you whether there is any problem, caution, or dosage issue in someone over 60 years old using the drug. Parts 1 and 2 of the guide can be used in conjunction with the main drug profiles to give more in-depth information about how groups of drugs work and how to use them. There are also updated sections on vitamins and minerals, drugs of abuse, complementary and alternative medicine, drugs in sport, and travel medicine.

As in other areas of medicine, information about drugs changes rapidly as new discoveries are made about existing drugs or new medications are introduced and so this guide is not meant to replace advice given by your doctor, pharmacist, or other health professional. We feel, however, that the information provided here will help you to work in partnership with your health advisors to use medicines and look after your health both safely and effectively.

Dr. Michael Peters
BMA Consulting Medical Editor

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INTRODUCTION

The British Medical Association New Guide to Medicines and Drugs has been planned and written to provide clear information and practical advice on drugs and medicines in a way that can be readily understood by a non-medical reader. The text reflects current medical knowledge and standard medical practice in this country. It is intended to complement and reinforce the advice given by your doctor, pharmacist, or other prescriber.

How the book is structured

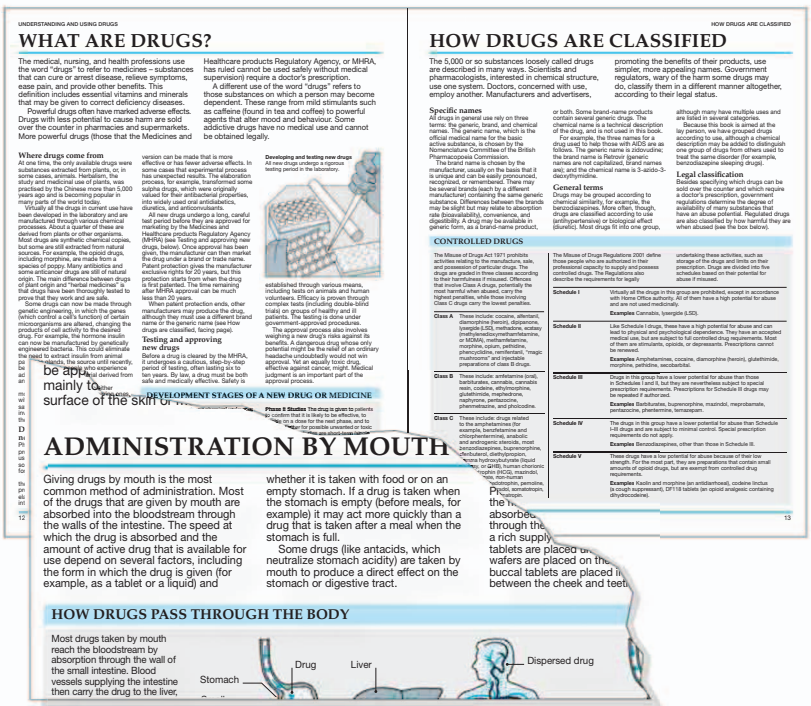
The book is divided into four parts. The first part, Understanding and Using Drugs, provides a general introduction to the effects of drugs and gives advice on practical questions, such as administration and storage of drugs. Part 2, Major Drug Groups, will help you to understand the uses and mechanisms of action of the principal classes of drugs. Part 3, the A–Z of Drugs, consists of 278 detailed profiles of commonly prescribed generic drugs, profiles of vitamins, minerals, and drugs of abuse, and information on complementary and alternative medicines, drugs in sport, and medicines and travel. Part 4 contains useful resources, a glossary of drug-related terms, the drug finder, which helps locate information on specific drugs through an index to over 2,500 generic and brand-name drugs, and a general index.

Finding your way into the book

The information you require, whether on the specific characteristics of an individual drug or on the general effects and uses of a group of drugs, can be easily obtained without prior knowledge of the medical names of drugs or drug classification through one of the two indexes: the drug finder or the general index. The diagram on the facing page shows how you can obtain information throughout the book on the subject concerning you from each of these starting points.

1 UNDERSTANDING AND USING DRUGS

The introductory part of the book, Understanding and Using Drugs, gives a grounding in the fundamental principles underlying the medical use of drugs. Covering such topics as classifications of drugs, mechanisms of action, and the proper use of medicines, it provides valuable background information that backs up the more detailed descriptions and advice given in Parts 2 and 3. You should read this section before seeking further specific information.



UNDERSTANDING AND USING DRUGS

WHAT ARE DRUGS?

The medical, nursing, and health professions use the word "drugs" to refer to medicines – substances that can cure or arrest disease, relieve symptoms, ease pain, and provide other benefits. This definition includes essential vitamins and minerals that may be given to correct deficiency diseases.

Powerful drugs often have marked adverse effects. Drugs with less potential to cause harm are sold over the counter in pharmacies and supermarkets. More powerful drugs (those that the Medicines and Healthcare products Regulatory Agency, or MHRA, has ruled cannot be used safely without medical supervision) require a doctor's prescription.

A different use of the word "drugs" refers to those substances on which a person may become dependent. These range from mild stimulants such as caffeine (found in tea and coffee) to powerful agents that alter mood and behaviour. Some addictive drugs have no medical use and cannot be obtained legally.

Where drugs come from

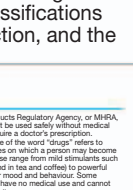
At one time, the only available drugs were substances extracted from plants, or, in some cases, animals. Herbalism, the study and medicinal use of plants, was practised by the Chinese more than 5,000 years ago, and remains popular in many parts of the world today.

Virtually all the drugs in current use have been developed in the laboratory and are manufactured through various chemical processes. About a quarter of these are derived from plants or other organisms. Most drugs are synthetic chemical copies, but some are still extracted from natural sources. For example, the opioid drugs, including morphine, are made from a substance found in the opium poppy, and some anticancer drugs are still of natural origin. The main difference between drugs of "plant origin and "herbal medicines" is that drugs have been thoroughly tested to prove that they work and are safe.

Some drugs can now be made through genetic engineering, in which the genes (which control a cell's function) of certain microorganisms are altered, changing the products of cell activity to the desired drug. For example, the hormone insulin can now be manufactured by genetically engineered bacteria. This is a considerable the need to extract insulin from animal pa... be ap... mainly to... surface of the skin or ...

Developing and testing new drugs

All new drugs undergo a rigorous testing period in the laboratory.



version can be made that is more effective or has fewer adverse effects. In some cases that experimental process has unexpected results. The elaboration process, for example, transformed some sulpha drugs, which were originally developed as antibacterial substances, into widely used oral antidiabetics, diuretics, and anticonvulsants.

All new drugs undergo a long, careful test period before they are approved for marketing by the Medicines and Healthcare products Regulatory Agency (MHRA) (see Testing and approving new drugs, below). Once approval has been given, the manufacturer can then market the drug under a brand or trade name. Normally, a company has a 20-year exclusive rights for 20 years, but this protection starts from when the drug is first patented. The time remaining after MHRA approval can be much less than 20 years.

When patent protection ends, other manufacturers may produce the drug, although they must use a different brand name or the generic name (see How drugs are classified, facing page).

Testing and approving new drugs

Before a drug is cleared by the MHRA, it undergoes a cautious, step-by-step period of testing, often lasting six to ten years. By law, a drug must be both safe and medically effective. Safety is established through various means, including tests on animals and human volunteers. Efficacy is proven through complex tests (including double-blind trials) on groups of healthy and ill patients. The testing is done under government-approved procedures.

The approval process also involves weighing a new drug's risks against its benefits. A dangerous drug whose only benefit is to relieve a fairly unimportant headache undoubtedly would not win approval. Yet an equally toxic drug, effective against cancer, might. Medical judgment is an important part of the approval process.

DEVELOPMENT STAGES OF A NEW DRUG OR MEDICINE

Phase II Studies The drug is given to patients to confirm that it is likely to be effective, to ... the drug in the next phase, and to ... for possible unwanted or toxic ...

HOW DRUGS ARE CLASSIFIED

The 5,000 or so substances loosely called drugs are described in many ways. Scientists and pharmacologists, interested in chemical structure, use one system. Doctors, concerned with use, employ another. Manufacturers and advertisers, promoting the benefits of their products, use simpler, more appealing names. Government regulators, wary of the harm some drugs may do, classify them in a different manner altogether, according to their legal status.

Specific names

All drugs in general use rely on three terms: the generic, brand, and chemical names. The generic name, which is the official medical name for the basic active substance, is chosen by the Nomenclature Committee of the British Pharmacopoeia Commission.

The brand name is chosen by the manufacturer, usually on the basis that it is unique and can be easily pronounced, recognized, or remembered. There may be several brands (each by a different manufacturer) available for the same generic substance. Differences between the brands may be slight but may relate to absorption rate (bioavailability), convenience, and digestibility. A drug may be available in generic form, as a brand-name product, or both. Some brand-name products contain several generic drugs. The chemical name is a technical description of the drug, and is not used in this book.

For example, the three names for a drug used to help those with AIDS are as follows. The generic name is zidovudine; the brand name is Retrovir (generic names are not capitalized, brand names are); and the chemical name is 3-azido-3-deoxythymidine.

General terms

Drugs may be grouped according to chemical similarity, for example, the benzodiazepines. More often, though, drugs are classified according to use (antihypertensive) or biological effect (diuretic). Most drugs fit into one group, although many have multiple uses and are listed in several categories.

Because this book is aimed at the lay person, we have grouped drugs according to use, although a chemical description may be added to distinguish one group of drugs from others used to treat the same disorder (for example, benzodiazepine sleeping drugs).

Legal classification

Classes specifying which drugs can be sold over the counter and which require a doctor's prescription; government regulations determine the degree of availability of many substances that have an abuse potential. Regulated drugs are also classified by how harmful they are when abused (see the box below).

CONTROLLED DRUGS

The Misuse of Drugs Act 1971 prohibits activities relating to the manufacture, sale, and possession of particular drugs. The drugs are graded in three classes according to the severity of penalties applicable to that involve Class A drugs, potentially the most harmful when abused, carry the highest penalties, while those involving Class C drugs carry the lowest penalties.

Class A These include: cocaine, afentanil, alfentanil, diamorphine (heroin), dipipanone (pyrogate (LSD), methadone, ecstasy (methylenedioxymethamfetamine, or MDMA), methamfetamine, morphine, opium, pethidine, phencyclidine, remifentanil, "magic mushrooms" and injectable preparations of class B drugs.

Class B These include: amfetamine (oral), barbiturates, cannabis, cannabis resin, codeine, ethylmorphine, glutethimide, meprhidrine, naphyrone, pentazocine, phenmetrazine, and phocodine.

Class C These include: drugs related to the amfetamines (for example, benzfetamine and chlorphentermine), anabolic and androgenic steroids, most barbiturates (for example, amobarbitone, butobarbitone), diethylpropion ...mma hydroxybutyrate (liquid ecstasy or GHB), human chorionic ...rophin (HCG), mazindol, ... Tess, non-human ... Diconophin, pemoline, ... and temazepam, ... and zopiclone.

The Misuse of Drugs Regulations 2001 define those people who are authorized in their professional capacity to supply and possess controlled drugs. The Regulations also describe the requirements for legally undertaking these activities, such as storage of the drugs and limits on their prescription. Drugs are divided into five schedules based on their potential for abuse if misused.

Schedule I Virtually all the drugs in this group are prohibited, except in accordance with Home Office authority. All of them have a high potential for abuse and are not used medicinally.

Examples Cannabis, lysergide (LSD).

Schedule II Like Schedule I drugs, these have a high potential for abuse and can lead to physical and psychological dependence. They have an accepted medical use, but are subject to full controlled drug requirements. Most of them are stimulants, opioids, or depressants. Prescriptions cannot be renewed.

Examples Amphetamines, cocaine, diamorphine (heroin), glutethimide, morphine, pethidine, secobarbital.

Schedule III Drugs in this group have a lower potential for abuse than those in Schedules I and II, but they are nevertheless subject to special prescription requirements. Prescriptions for Schedule III drugs may be repeated if authorized.

Examples Barbiturates, buprenorphine, mazindol, meprobamate, pentazocine, phentermine, temazepam.

Schedule IV The drugs in this group have a lower potential for abuse than Schedule I–III drugs and are subject to minimal control. Special prescription requirements do not apply.

Examples Benzodiazepines, other than those in Schedule III.

Schedule V These drugs have a low potential for abuse because of their low strength. For the most part, they are preparations that contain small amounts of opioid drugs, but are exempt from controlled drug requirements.

Examples Kaolin and morphine (an antidiarrhoeal), codeine linctus (a cough suppressant), DF118 tablets (an opioid analgesic containing dihydrocodeine).

ADMINISTRATION BY MOUTH

Giving drugs by mouth is the most common method of administration. Most of the drugs that are given by mouth are absorbed into the bloodstream through the walls of the intestine. The speed at which the drug is absorbed and the amount of active drug that is available for use depend on several factors, including the form in which the drug is given (for example, as a tablet or a liquid) and whether it is taken with food or on an empty stomach. If a drug is taken when the stomach is empty (before meals, for example) it may act more quickly than a drug that is taken after a meal when the stomach is full.

Some drugs (like antacids, which neutralize stomach acidity) are taken by mouth to produce a direct effect on the stomach or digestive tract.

... the ... absorbed ... through the ... a rich supply ... tablets are placed on ... wafers are placed on the ... buccal tablets are placed ... between the cheek and teet...

HOW DRUGS PASS THROUGH THE BODY

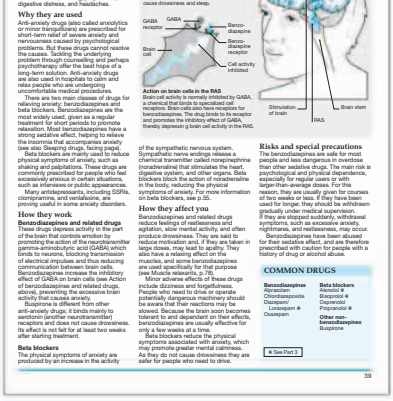
Most drugs taken by mouth reach the bloodstream by absorption through the wall of the small intestine. Blood vessels supplying the intestine then carry the drug to the liver,

12

13

2 MAJOR DRUG GROUPS

Subdivided into sections dealing with each body system (for example, heart and circulation) or major disease grouping (for example, malignant and immune disease), this part of the book contains descriptions of the principal classes of drugs. Information is given on the uses, actions, effects, and risks associated with each group of drugs and is backed up by helpful illustrations and diagrams. Individual drugs in each group are listed to allow cross-reference to Part 3.



BRAIN AND NERVOUS SYSTEM

ANTI-ANXIETY DRUGS

A certain amount of stress can be beneficial, providing a stimulus to action. But too much will often result in anxiety, which might be described as fear or apprehension not caused by real danger. Anxiety is a symptom that the delicate balance of certain chemicals in the brain is disturbed. The fearful feelings increase brain activity, stimulating the sympathetic nervous system (see p.35), and often triggers physical symptoms, for example, breathlessness, shaking, palpitations, digestive distress, and headaches.

ACTION OF BENZODIAZEPINES AND RELATED DRUGS

Action on the brain

The reticular activating system (RAS) in the brain stem controls the level of mental activity by stimulating higher centres of the brain (cerebral hemispheres). Benzodiazepines and related drugs depress the RAS, relieving anxiety. In larger doses they depress the RAS sufficiently to cause drowsiness and sleep.

Action on brain cells in the RAS

Brain cell activity is normally inhibited by GABA, a chemical that binds to specialized cell receptors. Brain cells have two receptors for GABA: one for the drug itself, the GABA receptor, and promotes the inhibitory effect of GABA, thereby depressin g brain cell activity in the RAS.

How they work

Benzodiazepines and related drugs

These drugs depress activity in the part of the brain that controls emotion by promoting the action of the neurotransmitter gamma-aminobutyric acid (GABA) which in turn reduces the transmission of electrical impulses and thus reducing communication between brain cells. Benzodiazepines increase the inhibitory effect of GABA on brain cells (see Action of benzodiazepines and related drugs, above), preventing the excessive brain activity that causes anxiety.

Buspirone is different from other anti-anxiety drugs. It binds mainly to serotonin (another neurotransmitter) receptors and does not cause drowsiness. Its effect is not felt for at least two weeks after starting treatment.

Beta blockers

The physical symptoms of anxiety are produced by an increase in the activity of the sympathetic nervous system. Sympathetic nerve endings release a chemical transmitter called noradrenaline (noradrenaline) that stimulates the heart, digestive system, and other organs. Beta blockers block the action of noradrenaline in the body, reducing the physical symptoms of anxiety. For more information on beta blockers, see p.35.

How they affect you

Benzodiazepines and related drugs reduce feelings of restlessness and agitation, slow mental activity, and often produce drowsiness. They are said to reduce motivation and, if they are taken in large doses, may lead to apathy. They relax the tension in the body's muscles, and some benzodiazepines are used specifically for that purpose (see Muscle relaxants, p.78).

Minor adverse effects of these drugs include dizziness and forgetfulness. People who need to drive or operate potentially dangerous machinery should be aware that their reactions may be slowed. Although a person becomes tolerant to and dependent on their effects, benzodiazepines are usually effective for only a few weeks at a time.

Beta blockers reduce the physical symptoms associated with anxiety, which may promote greater mental calmness. As they do not cause drowsiness they are safer for people who need to drive.

Risks and special precautions

The benzodiazepines are safe for most people and less dangerous in overdose than other sedative drugs. The main risk is psychological and physical dependence, especially for regular users or with larger-than-average doses. For this reason, they are usually given for courses of no more than four weeks. If they have been used for longer, they should be withdrawn gradually under medical supervision. If they are stopped suddenly, withdrawal symptoms, such as excessive anxiety, nightmares, and restlessness, may occur.

Benzodiazepines have been abused for their sedative effect, and are therefore prescribed with caution for people with a history of drug or alcohol abuse.

COMMON DRUGS

Benzodiazepines
Alprazolam
Chlordiazepoxide
Diazepam*
Lorazepam ✱
Oxazepam

Beta blockers
Atenolol ✱
Bisoprolol ✱
Oxprenolol
Propranolol ✱

Other non-benzodiazepines
Buspirone

✱ See Part 3

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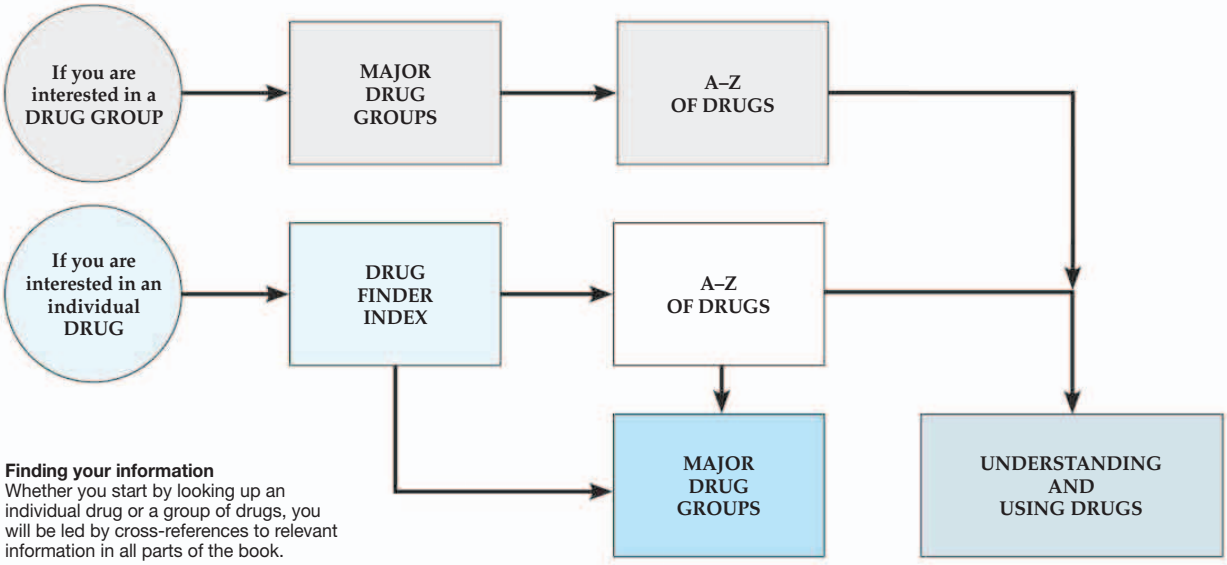
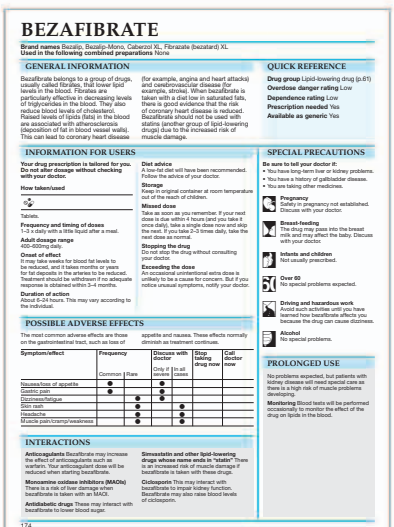

If you are interested in a DRUG GROUP
MAJOR DRUG GROUPS
A–Z OF DRUGS
If you are interested in an individual DRUG
DRUG FINDER INDEX
A–Z OF DRUGS
MAJOR DRUG GROUPS
UNDERSTANDING AND USING DRUGS

Finding your information
Whether you start by looking up an individual drug or a group of drugs, you will be led by cross-references to relevant information in all parts of the book.

3 A–Z OF DRUGS

In this part, standard-format profiles of 278 generic drugs help you to find specific information quickly and easily; cross-references to relevant major drug groups are also provided. Supplementary sections cover vitamins and minerals, drugs of abuse, complementary and alternative medicine, drugs in sport, and medicines and travel.



BEZAFIBRATE

Brand names Bezalip, Bezalip-Mono, Cabenzol XL, Fibrazate (bezafibrate) XL
Used in the following combined preparations None

GENERAL INFORMATION

Bezafibrate belongs to a group of drugs, usually called fibrates, that lower lipid levels in the blood. Fibrates are particularly effective in decreasing levels of triglycerides in the blood. They also reduce blood levels of cholesterol. Cholesterol and fats in the blood are associated with atherosclerosis (deposition of fat in blood vessel walls). This can lead to coronary heart disease (for example, angina and heart attacks) and cerebrovascular disease (for example, stroke). When bezafibrate is taken with a diet low in saturated fats, there is good evidence that the risk of coronary heart disease is reduced. Bezafibrate is also used in people for whom statins (another group of lipid-lowering drugs) due to the increased risk of muscle damage.

QUICK REFERENCE

Drug group Lipid-lowering drug (p.61)
Overdose danger rating Low
Dependence rating Low
Prescription needed Yes
Available as generic Yes

INFORMATION FOR USERS

Your drug prescription is tailored for you. Do not alter dosage without checking with your doctor.

How taken/used

Tablets.

Frequency and timing of doses
1–3 a daily with a little liquid after a meal.

Adult dosage range
400–600mg daily.

Onset of effect
It may take weeks for blood fat levels to be reduced, and it takes months or years for fat deposits in the arteries to be reduced. Treatment should be withdrawn if no adequate response is obtained within 3–4 months.

Duration of action
About 8–24 hours. This may vary according to the individual.

Diet advice
A low-fat diet will have been recommended. Follow the advice of your doctor.

Storage
Keep in original container at room temperature out of the reach of children.

Missed dose
Take as soon as you remember. If your next dose is due within 4 hours (and you take it once daily), take a single dose now and skip the next. If you take 2–3 times daily, take the next dose as normal.

Stopping the drug
Do not stop the drug without consulting your doctor.

Exceeding the dose
An occasional unintentional extra dose is unlikely to be a cause for concern. But if you notice unusual symptoms, notify your doctor.

SPECIAL PRECAUTIONS

Be sure to tell your doctor if:
- You have long-term liver or kidney problems.
- You have a history of gallbladder disease.
- You are taking other medicines.

Pregnancy
Safety in pregnancy not established. Discuss with your doctor.

Breast-feeding
The drug may pass into the breast milk and may affect the baby. Discuss with your doctor.

Infants and children
Not usually prescribed.

Over 60
No special problems expected.

Driving and hazardous work
Avoid such activities until you have learned how bezafibrate affects you because the drug can cause dizziness.

Alcohol
No special problems.

POSSIBLE ADVERSE EFFECTS

The most common adverse effects are those on the gastrointestinal tract, such as loss of appetite and nausea. These effects normally diminish as treatment continues.

Symptom/effect	Frequency		Discuss with doctor		Stop taking drug now	Call doctor now
	Common	Rare	Only if in all cases	If severe		
Nausea/loss of appetite	●		●			
Gastric pain	●		●			
Dizziness/fatigue		●	●			
Skin rash		●		●		
Headache		●		●		
Muscle pain/cramp/weakness		●		●		

PROLONGED USE

No problems expected, but patients with kidney disease will need special care as there is a high risk of muscle problems developing.

Monitoring Blood tests will be performed occasionally to monitor the effect of the drug on lipids in the blood.

INTERACTIONS

Anticoagulants Bezafibrate may increase the effect of anticoagulants such as warfarin. Your anticoagulant dose will be reduced when starting bezafibrate.

Monoamine oxidase inhibitors (MAOIs) There is a risk of liver damage when bezafibrate is taken with an MAOI.

Antidiabetic drugs These may interact with bezafibrate to lower blood sugar.

Simvastatin and other lipid-lowering drugs whose name ends in 'statin' There is an increased risk of muscle damage if bezafibrate is taken with these drugs.

Ciclosporin This may interact with bezafibrate to impair kidney function. Bezafibrate may also raise blood levels of ciclosporin.

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4 INFORMATION AND INDEX

Useful resources, including websites, direct you to further information; the glossary explains technical words; the drug finder helps you to find information on specific brand-name drugs and generic substances; and the index enables you to look up references throughout the book.

GLOSSARY

GLOSSARY

The following pages contain definitions of drug-related terms whose technical meanings are not explained in detail elsewhere in the book, or for which an easily located precise explanation may be helpful. These are words that may not be familiar to the general reader, or that have a slightly different meaning in a medical context from that in ordinary use. Some of the terms included refer to particular drug actions or effects; others describe methods of drug administration. A few medical conditions that may occur as a result of drug use are also defined.

The glossary is arranged in alphabetical order. To avoid repetition, where relevant, entries include cross-references to further information on that topic located in other sections of the book, or to another glossary term (indicated by italics).

A

Activator
See *Agonist*.

Addiction
A term referring to compulsive use of a drug that can cover anything from intense, habitual cravings for caffeine (the drug in coffee and tea) to physical and psychological dependence on drugs such as nicotine (in tobacco) and *heroin*. See also Dependence and Drug dependence (p.24).

Adjuvant
A drug or chemical that enhances the therapeutic effect of another drug. An example is aluminium, which is added to certain *vaccines* to enhance the immune responses, thereby increasing the protection that is given by the vaccine.

Adrenergic
See *Sympathomimetic*.

Adverse effect
Like side effect and adverse reaction, this is a term that refers to unwanted effects of a drug. When drugs are taken they are distributed throughout the body and their actions are unlikely to be restricted to just the intended organ or tissue. Another part of the body contain receptors for the drug and so it has an effect. The drug molecule may fit other, different receptors well enough to affect them too. Most of these unwanted effects are dose-related, increasing as the dose is increased. Other unwanted adverse effects appear not to be dose-related, such as an idiosyncrasy or an allergic reaction. See also Adverse effects (p. 15).

Adverse reaction
See *Adverse effect*.

Agonist
A term meaning to have a stimulating effect. The term is usually applied to a drug or *hormone* that binds to a receptor, and activates it. This may trigger an increase or decrease in particular activity in that cell depending on the physiological effects of activating that particular receptor.

Allergic reaction
An allergic reaction or allergy is one that appears not on first exposure to a drug but on a subsequent occasion. The causes and symptoms are similar to a reaction caused by other allergens. See Allergy (p.97) and *Anaphylaxis*.

Amoebicide
A drug that kills amoebae (single-celled microorganisms). See also Antiprotozoal drugs (p.94).

Anaemia
A condition in which the concentration of the oxygen-carrying pigment of the blood, *haemoglobin*, is below normal. Many different disorders may cause anaemia, and it may sometimes occur as a result of drug treatment. Severe anaemia may cause fatigue, pallor, and occasionally, breathing difficulty.

Anaesthetic, general
A drug or drug combination given to produce unconsciousness before and during surgery or potentially painful investigative procedures. General anaesthesia is usually induced by injection of a drug such as thiopental or propofol, and then maintained by inhalation of gas mixtures of perhaps enflurane, nitrous oxide, and oxygen. Alternatively, general anaesthesia is also possible depending on the type and duration of operation for example with propofol. See also *Premedication*.

Anaesthetic, local
A drug applied topically or injected to numb sensation in a small area. See also Local anaesthetics (p.34).

Analeptic
A drug given in hospital that stimulates breathing. See also Respiratory stimulants (p.44).

Analgesia
Relief of pain, usually by drugs. See also Analgesics (p.36).

Anaphylaxis
A severe reaction to an allergen such as a bee sting, a food, or a drug. The effects of anaphylaxis may include rash, swelling, breathing difficulty, and collapse. See also Anaphylactic shock (p.510).

Antagonist
A term meaning to have an opposing effect. An antagonist drug usually blocks the action of a receptor without activating it and prevents any other substance from occupying and activating that receptor i.e. agonists.

Antibiotic
A substance that kills or arrests the growth of bacteria. Originally, antibiotics were produced by microorganisms, but nowadays most are now produced synthetically. See also Antibiotics (p.66), Antifungal drugs (p.96), and Antibacterial drugs (p.66).

Antibody
A protein manufactured by lymphocytes (a type of white blood cell) to neutralize an antigen (foreign protein) in the body. The formation of antibodies to specific antigens (immunization) is part of the body's defence against infection. Immunization carried out to increase the body's resistance to a specific disease involves either injection of specific antibodies or administration of a vaccine that stimulates antibody production. See also Vaccines and Immunization (p.93).

Anticholinergic
A drug that blocks the action of acetylcholine. Acetylcholine, a neurotransmitter secreted by the endings of nerve cells, allows certain nerve impulses to be transmitted, including those that control the heart, gastrointestinal tract, glands, and affect the release of saliva. Anticholinergic drugs are used to treat urinary incontinence because they relax the bladder's squeezing muscles while tightening those of the sphincter. Anticholinergic drugs also relax the muscles of the intestinal wall, helping to relieve irritable bowel syndrome (p.56). See also Autonomic nervous system (p.20).

Antidote
A substance used to neutralize or counteract the effects of a poison. A few poisons have a specific antidote e.g. morphine is specifically blocked by naloxone.

Antineoplastic
An anticancer drug (p.114).

Antioxidant
A substance that delays deterioration due to oxidation (reaction with oxygen). Many free radicals are generated by the body's normal processes and are thought to play a role in aging and disease. Vitamins A, C, and E are antioxidants. See also Vitamins (p.107).

Antiperspirant
A substance applied to the skin to reduce excess sweating. Antiperspirants reduce the activity of the sweat glands or block ducts carrying sweat to the skin surface.

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DRUG FINDER

This section contains the names of more than 2,500 individual drug products and substances. It provides a quick and easy reference for readers interested in finding out about a specific drug or medication. There is no need for you to know whether the item is a brand name or generic drug, or whether it is a prescription or over-the-counter drug: all types of drug are listed.

This con
diversity
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product
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indicate

What it contains

The drugs are listed alphabetically and include all major generic drugs and many less widely used substances. A broad range of brand names, as well as many vitamins and minerals, are also included.

How th

Referenc
the drug
and to the section in Part 2 that describes the relevant drug group, as appropriate. Some entries for generic drugs that do not have a full profile contain a brief description here.

A

abacavir an antiretroviral for HIV/AIDS 116
abatacept a cytokine modulator antirheumatic drug 75 used to treat moderate to severe rheumatoid arthritis
abciximab an antiplatelet drug 62
Abelcet a brand name for amphotericin 160 (an antifungal 96)
Abidec a brand-name multivitamin 107
Abilify a brand name for aripiprazole (an antipsychotic 41)
Abraxane a brand name for paclitaxel (an anticancer drug 112)
Abstral a brand name for fentanyl (an opioid analgesic 36)
acamprosate a dru for alcohol abuse 440 used in addition to counselling
acarbose an oral antidiabetic 100
Accolate a brand name for zafirlukast (a leukotriene receptor antagonist for asthma 49 and bronchospasm 48)
Accrete D3 a brand name for vitamin [illegible]7 (a vitamin 107) with calcium carbo[illegible]
sal[illegible]

Acidex a brand-name preparation containing an alginate 150 used to treat indigestion
acipimox a lipid-lowering drug 61
acitretin a drug for psoriasis 138
Aclasta a brand name for zoledronic acid 424 (a drug for bone disorders 80)
Acnecide a brand name for benzoyl peroxide 170 (a drug for acne 137)
Acnisal a brand name for salicylic acid (a drug for acne 137)
Acnocin a brand name for co-cyprindiol, a combined preparation of cyproterone 215 and ethinylestradiol 246 used to treat acne 137
acrivastine an antihistamine 82
Actifed Chesty Coughs a brand name for guaifenesin (an expectorant 52) with pseudoephedrine (a decongestant 51) and triprolidine (an antihistamine 82)
Actifed Dry Coughs a brand name for dextromethorphan (a cough suppressant 52) with pseudoephedrine (a decongestant 51) and triprolidine (an antihistamine 82)
Actikerall a brand name for 5-fluorouracil with salicylic acid (drugs for actinic keratosis)
Actilyse a brand name for alteplase 15[illegible]

ACWY Vax a brand-name vaccine 92 to protect againt meningococcal infections
Adalat a brand name for nifedipine 334 (a calcium-channel blocker anti-anging drug 59 and antihypertensive 60)
Adalat Retard a brand name for a modified release preparation of nifedipine 334 (a calcium-channel blocker, anti-anging drug 59, and antihypertensive 60)
adalimumab a disease-modifying antirheumatic drug 75
adapalene a retinoid for acne 137
Adartrel a brand-name drug for restless legs containing ropinirole 380
Adcal D3 a brand name for calcium carbonate 427 (a mineral 107) with vitamin D 437 (a vitamin 107)
Adcortyl a brand name for triamcinolone (a corticosteroid 99)
adefovir an antiviral 91 for chronic hepatiti[illegible]
Adenocor a brand name for adeno[illegible]
arrhythmic 58)

PART

1

UNDERSTANDING AND USING DRUGS

WHAT ARE DRUGS?
HOW DRUGS ARE CLASSIFIED
HOW DRUGS WORK
METHODS OF ADMINISTRATION
DRUG TREATMENT IN SPECIAL RISK GROUPS
DRUG TOLERANCE AND DEPENDENCE
MANAGING YOUR DRUG TREATMENT

WHAT ARE DRUGS?

The medical, nursing, and health professions use the word "drugs" to refer to medicines – substances that can cure or arrest disease, relieve symptoms, ease pain, and provide other benefits. This definition includes essential vitamins and minerals that may be given to correct deficiency diseases.

Powerful drugs often have marked adverse effects. Drugs with less potential to cause harm are sold over the counter in pharmacies and supermarkets. More powerful drugs (those that the Medicines and Healthcare products Regulatory Agency, or MHRA, has ruled cannot be used safely without medical supervision) require a doctor's prescription.

A different use of the word "drugs" refers to those substances on which a person may become dependent. These range from mild stimulants such as caffeine (found in tea and coffee) to powerful agents that alter mood and behaviour. Some addictive drugs have no medical use and cannot be obtained legally.

Where drugs come from

At one time, the only available drugs were substances extracted from plants, or, in some cases, animals. Herbalism, the study and medicinal use of plants, was practised by the Chinese more than 5,000 years ago and is becoming popular in many parts of the world today.

Virtually all the drugs in current use have been developed in the laboratory and are manufactured through various chemical processes. About a quarter of these are derived from plants or other organisms. Most drugs are synthetic chemical copies, but some are still extracted from natural sources. For example, the opioid drugs, including morphine, are made from a species of poppy. Many antibiotics and some anticancer drugs are still of natural origin. The main difference between drugs of plant origin and "herbal medicines" is that drugs have been thoroughly tested to prove that they work and are safe.

Some drugs can now be made through genetic engineering, in which the genes (which control a cell's function) of certain microorganisms are altered, changing the products of cell activity to the desired drug. For example, the hormone insulin can now be manufactured by genetically engineered bacteria. This could eliminate the need to extract insulin from animal pancreas glands, the source until recently, benefiting those people who experience adverse reactions to material derived from animal sources.

Purely synthetic drugs are either modifications of naturally occurring ones, with the aim of increasing effectiveness or safety, or drugs developed after scientific investigation of a disease process with the intention of changing it biochemically.

Developing and marketing new drugs

Pharmaceutical manufacturers find new products in various ways. New drugs are usually developed for one purpose but sometimes a variant is found to be useful for something different.

When a new drug is discovered, the manufacturer often undertakes a programme of molecular tinkering, or elaboration. This refers to investigations into variants of the drug to see if a version can be made that is more effective or has fewer adverse effects. In some cases that experimental process has unexpected results. The elaboration process, for example, transformed some sulpha drugs, which were originally valued for their antibacterial properties, into widely used oral antidiabetics, diuretics, and anticonvulsants.

All new drugs undergo a long, careful test period before they are approved for marketing by the Medicines and Healthcare products Regulatory Agency (MHRA) (see Testing and approving new drugs, below). Once approval has been given, the manufacturer can then market the drug under a brand or trade name. Patent protection gives the manufacturer exclusive rights for 20 years, but this protection starts from when the drug is first patented. The time remaining after MHRA approval can be much less than 20 years.

When patent protection ends, other manufacturers may produce the drug, although they must use a different brand name or the generic name (see How drugs are classified, facing page).

Testing and approving new drugs

Before a drug is cleared by the MHRA, it undergoes a cautious, step-by-step period of testing, often lasting six to ten years. By law, a drug must be both safe and medically effective. Safety is established through various means, including tests on animals and human volunteers. Efficacy is proven through complex tests (including double-blind trials) on groups of healthy and ill patients. The testing is done under government-approved procedures.

The approval process also involves weighing a new drug's risks against its benefits. A dangerous drug whose only potential might be the relief of an ordinary headache undoubtedly would not win approval. Yet an equally toxic drug, effective against cancer, might. Medical judgment is an important part of the approval process.

Developing and testing new drugs
All new drugs undergo a rigorous testing period in the laboratory.

DEVELOPMENT STAGES OF A NEW DRUG OR MEDICINE

Discovery Stage A new chemical undergoes thorough chemical and biological study. If these tests suggest it has promise as a new drug, the process of drug development starts.

Preclinical Studies The first stage of research on a new chemical includes testing on isolated organs and tissues and animal studies. These tests are required before permission can be granted for human clinical trials.

Phase I Studies This is the first stage of testing on human subjects, which usually consist of small groups of healthy volunteers, or sometimes patients. The aim is to assess both the safety of the chemical and how the body deals with it.

Phase II Studies The drug is given to patients to confirm that it is likely to be effective, to decide on a dose for the next phase, and to monitor further for possible unwanted or toxic effects. These studies are short-term (single doses or regular dosing for several weeks).

Phase III Studies Large-scale human studies are carried out to gather sufficient evidence of the drug's efficacy and safety to gain marketing approval. They must be long-term (about a year) double-blind, multi-centre, controlled trials.

Phase IV Studies Once the drug is on the market, further monitoring studies are needed to provide ongoing evidence of its overall effectiveness, safety and usefulness.

HOW DRUGS ARE CLASSIFIED

The 5,000 or so substances loosely called drugs are described in many ways. Scientists and pharmacologists, interested in chemical structure, use one system. Doctors, concerned with use, employ another. Manufacturers and advertisers, promoting the benefits of their products, use simpler, more appealing names. Government regulators, wary of the harm some drugs may do, classify them in a different manner altogether, according to their legal status.

Specific names

All drugs in general use rely on three terms: the generic, brand, and chemical names. The generic name, which is the official medical name for the basic active substance, is chosen by the Nomenclature Committee of the British Pharmacopoeia Commission.

The brand name is chosen by the manufacturer, usually on the basis that it is unique and can be easily pronounced, recognized, or remembered. There may be several brands (each by a different manufacturer) containing the same generic substance. Differences between the brands may be slight but may relate to absorption rate (bioavailability), convenience, and digestibility. A drug may be available in generic form, as a brand-name product, or both. Some brand-name products contain several generic drugs. The chemical name is a technical description of the drug, and is not used in this book.

For example, the three names for a drug used to help those with AIDS are as follows. The generic name is zidovudine; the brand name is Retrovir (generic names are not capitalized, brand names are); and the chemical name is 3-azido-3-deoxythymidine.

General terms

Drugs may be grouped according to chemical similarity, for example, the benzodiazepines. More often, though, drugs are classified according to use (antihypertensive) or biological effect (diuretic). Most drugs fit into one group, although many have multiple uses and are listed in several categories.

Because this book is aimed at the lay person, we have grouped drugs according to use, although a chemical description may be added to distinguish one group of drugs from others used to treat the same disorder (for example, benzodiazepine sleeping drugs).

Legal classification

Besides specifying which drugs can be sold over the counter and which require a doctor's prescription, government regulations determine the degree of availability of many substances that have an abuse potential. Regulated drugs are also classified by how harmful they are when abused (see the box below).

CONTROLLED DRUGS

The Misuse of Drugs Act 1971 prohibits activities relating to the manufacture, sale, and possession of particular drugs. The drugs are graded in three classes according to their harmfulness if misused. Offences that involve Class A drugs, potentially the most harmful when abused, carry the highest penalties, while those involving Class C drugs carry the lowest penalties.

Class A	These include: cocaine, alfentanil, diamorphine (heroin), dipipanone, lysergide (LSD), methadone, ecstasy (methylenedioxymethamfetamine, or MDMA), methamfetamine, morphine, opium, pethidine, phencyclidine, remifentanil, "magic mushrooms" and injectable preparations of class B drugs.
Class B	These include: amfetamine (oral), barbiturates, cannabis, cannabis resin, codeine, ethylmorphine, glutethimide, mephedrone, naphyrone, pentazocine, phenmetrazine, and pholcodine.
Class C	These include: drugs related to the amphetamines (for example, benzfetamine and chlorphentermine), anabolic and androgenic steroids, most benzodiazepines, buprenorphine, clenbuterol, diethylpropion, gamma hydroxybutyrate (liquid ecstasy, or GHB), human chorionic gonadotrophin (HCG), mazindol, meprobamate, non-human chorionic gonadotrophin, pemoline, phenbuterol, pipradol, somatotropin, somatrem, and somatropin.

The Misuse of Drugs Regulations 2001 define those people who are authorized in their professional capacity to supply and possess controlled drugs. The Regulations also describe the requirements for legally undertaking these activities, such as storage of the drugs and limits on their prescription. Drugs are divided into five schedules based on their potential for abuse if misused.

Schedule I	Virtually all the drugs in this group are prohibited, except in accordance with Home Office authority. All of them have a high potential for abuse and are not used medicinally. **Examples** Cannabis, lysergide (LSD).
Schedule II	Like Schedule I drugs, these have a high potential for abuse and can lead to physical and psychological dependence. They have an accepted medical use, but are subject to full controlled drug requirements. Most of them are stimulants, opioids, or depressants. Prescriptions cannot be renewed. **Examples** Amphetamines, cocaine, diamorphine (heroin), glutethimide, morphine, pethidine, secobarbital.
Schedule III	Drugs in this group have a lower potential for abuse than those in Schedules I and II, but they are nevertheless subject to special prescription requirements. Prescriptions for Schedule III drugs may be repeated if authorized. **Examples** Barbiturates, buprenorphine, mazindol, meprobamate, pentazocine, phentermine, temazepam.
Schedule IV	The drugs in this group have a lower potential for abuse than Schedule I–III drugs and are subject to minimal control. Special prescription requirements do not apply. **Examples** Benzodiazepines, other than those in Schedule III.
Schedule V	These drugs have a low potential for abuse because of their low strength. For the most part, they are preparations that contain small amounts of opioid drugs, but are exempt from controlled drug requirements. **Examples** Kaolin and morphine (an antidiarrhoeal), codeine linctus (a cough suppressant), DF118 tablets (an opioid analgesic containing dihydrocodeine).

HOW DRUGS WORK

Before the discovery of the sulpha drugs in 1935, medical knowledge of drugs was limited to possibly only a dozen or so drugs that had a clear medical value. Most of these were the extracts of plants (such as digitalis, from foxgloves), while others, such as aspirin, were chemically closely related to plant extracts (in this case, salicylic acid, from the willow tree). It was soon realized, however, that crude plant extracts had two disadvantages: they were of variable potency, and the same plant could contain a number of different substances with different actions. These might even oppose each other, or cause serious adverse effects. Now, thousands of effective drugs are available and scientific knowledge regarding drugs and their actions has virtually exploded.

Today's doctor understands the complexity of drug actions in the body, both beneficial and adverse. As a result of extensive research and clinical experience, the doctor can now also recognize that some drugs interact harmfully with others, or with certain foods and alcohol.

DRUG ACTIONS

While the exact workings of some drugs are not fully understood, medical science provides clear knowledge as to what most of them do once they enter or are applied to the human body. Drugs serve different purposes: sometimes they cure a disease, sometimes they only alleviate symptoms. Their impact occurs in various parts of the anatomy. Although different drugs act in different ways, their actions generally fall into one of three categories.

Replacing chemicals that are deficient

To function normally, the body requires sufficient levels of certain chemical substances. These include vitamins and minerals, which the body obtains from food. A balanced diet usually supplies what is needed. But when deficiencies occur, various deficiency diseases result. Lack of vitamin C causes scurvy, iron deficiency causes anaemia, and lack of vitamin D leads to rickets in children and osteomalacia in adults.

Other deficiency diseases arise from a lack of various hormones which are the chemical substances produced by glands. Hormones act as internal messengers. Diabetes mellitus, hypothyroidism, and Addison's disease all result from deficiencies of different hormones.

Deficiency diseases are treated with drugs that replace the substances that are missing or, in the case of some hormone deficiencies, with animal or synthetic replacements.

Interfering with cell function

Many drugs can change the way cells work by increasing or reducing the normal level of activity. Inflammation, for example, is due to the action of certain natural hormones and other chemicals on blood vessels and blood cells. Anti-inflammatory drugs block the action of the hormones or slow their production. Drugs that act in a similar way are used in the treatment of a variety of conditions: hormone disorders, blood clotting problems, and heart and kidney diseases.

Many such drugs do their work by altering the transmission system by which messages are sent from one part of the body to another.

A message – to contract a muscle, say – originates in the brain and enters a nerve cell through its receiving end. The message, in the form of an electrical impulse, travels the nerve cell to the sending end. Here a chemical substance called a neurotransmitter is released, conducting the message across the tiny gap (synapse) separating it from an adjacent nerve cell. That process is repeated until the message reaches the appropriate muscle.

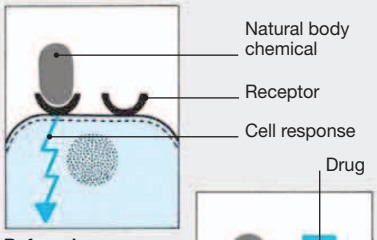
Many drugs can alter this process, often by their effect on receptor sites on cells (see left). Some drugs (agonists) intensify the response to cell receptor activation while other drugs (antagonists) reduce it.

Acting against invading organisms or abnormal cells

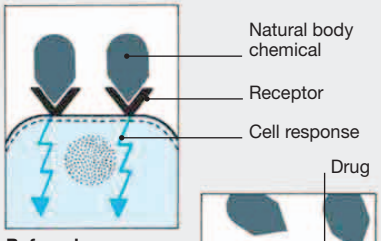
Infectious diseases are caused by viruses, bacteria, protozoa, and fungi invading the body. We now have a wide choice of drugs that destroy these microorganisms, either by halting their multiplication or by killing them directly. Other drugs treat disease by killing abnormal cells produced by the human body – cancer cells, for example.

RECEPTOR SITES

Many drugs produce their effects through their action on special sites called receptors, which may be on the surface of cells or inside them. Natural body chemicals such as neurotransmitters bind to these sites, initiating a response in the cell. A cell may have many types of receptors, each with an affinity for a different chemical. Drugs may also bind to receptors, either adding to the effect of the body's natural chemicals and enhancing cell response (agonists) or preventing such a chemical from binding to its receptor, and thereby blocking a particular cell response (antagonists).



Agonist drugs
These drugs bind to receptors and enhance normal cell response to receptor activation.



Antagonist drugs
These drugs bind to receptors and block cell response to receptor activation.

THE EFFECTS OF DRUGS

Before a doctor selects a drug to be used in the treatment of a sick person, he or she carefully weighs the benefits and the risks. Obviously, the doctor expects a positive result from the drug – a cure for the condition or at least the relief of symptoms. At the same time, the doctor has to consider the risks, since all drugs are potentially harmful, some of them considerably more so than others.

Reaction time

Some drugs can produce rapid and spectacular relief from the symptoms of disease. Glyceryl trinitrate frequently provides almost immediate relief from the pain of angina; other drugs can quickly alleviate the symptoms of an asthmatic attack. Conversely, some drugs take much longer to produce a response. It may, for example, require several weeks of treatment with an antidepressant drug before a person experiences maximum benefit. This can add to anxiety unless the doctor has warned of the possibility of a delay in the onset of beneficial effects.

Adverse effects

The adverse effects of a drug (also known as side effects or adverse reactions) are its undesired effects. When drugs are taken, they are distributed throughout the body and their effects are unlikely to be restricted just to the organ or tissue we want them to affect. Other parts of the body contain receptor sites like those the drug is targeting. In addition, the drug molecule may fit other, different receptors well enough to activate or block them too.

For example, anticholinergic drugs, given to relieve spasm of the intestinal wall, may also cause blurred vision, dry mouth, and retention of urine. Such effects may gradually disappear as the body becomes used to the drug. If they persist, the dose may have to be reduced, or the time between doses may need to be increased. Reducing the dose will often reduce the severity of the adverse effect for those effects that are called "dose-related".

DOSE AND RESPONSE

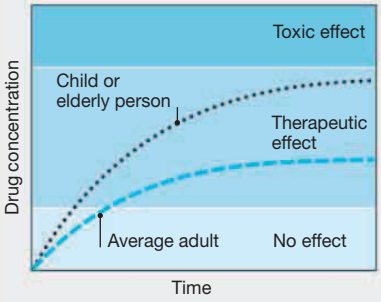
People respond in different ways to a drug, and often the dose has to be adjusted to allow for a person's age, weight, or general health.

The dose of any drug should be sufficient to produce a beneficial response but not so great that it will cause excessive adverse effects. If the dose is too low, the drug may not have any effect, either beneficial or adverse; if it is too high, it will not produce any additional benefits and may produce adverse effects.

The aim of drug treatment is to achieve a concentration of drug in the blood or tissue that lies between the minimum effective level and the maximum safe concentration. This is known as the therapeutic window (or range).

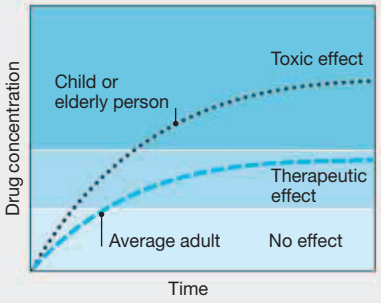
For certain drugs, such as digitalis drugs, the therapeutic window is quite narrow, so the margin of safety/effectiveness is small. Other drugs, such as penicillin antibiotics, have a much wider therapeutic window.

Wide therapeutic window



Dosage of drugs with a wide therapeutic window can vary considerably without altering the drug's effect. The effect is greater in children and the elderly.

Narrow therapeutic window



Dosage of drugs with a narrow therapeutic window must be carefully calculated to achieve the desired effect without toxicity. Children or the elderly experience toxic levels earlier.

Adverse effects of some drugs can be quite serious. Such drugs are given because they may be the only treatment for an otherwise fatal disease. But all drugs are chemicals, with a potential for producing serious, toxic reactions. Some adverse effects seem not to be dose-related, and where the effect appears on first use and is unexpected, the phenomenon is called idiosyncrasy. People are genetically different and, as a result, their response to drugs differs, perhaps because they lack a particular enzyme or because it is less active than usual. For this reason, not everybody suffers even the "common" adverse effects; but, occasionally, a new adverse effect, due to a rare and unsuspected genetic variation, will be discovered only after the drug has been taken by a large number of people.

Other adverse effects that are not dose-related are allergic reactions. These reactions do not usually appear on the first exposure to the drug but on a subsequent occasion. The symptoms are similar to those caused by other allergens and, in extreme cases, may cause anaphylactic shock (see p.512).

Beneficial vs. adverse effects

In evaluating the risk/benefit ratio of a prescribed drug, the doctor has to weigh the drug's therapeutic benefit to the sick person against the possible adverse effects. For example, such side effects as nausea, headache, and diarrhoea may result from taking an antibiotic. But the possible risks of the drug's side effects will certainly be considered acceptable if the problem is a life-threatening infection requiring immediate medical treatment. On the other hand, such side effects would be considered unacceptable for an over-the-counter drug for the relief of headaches.

Because some people are more at risk from adverse drug reactions than others (particularly those who have a history of drug allergy), the doctor normally checks whether there is any reason why a certain drug should not be prescribed (see Drug treatment in special risk groups, p.20).

PLACEBO RESPONSE

The word placebo – Latin for "I will please" – is used to describe any chemically inert substance given as a substitute for a drug. Any benefit gained from taking a placebo occurs because the person taking it believes that it will produce good results.

New drugs are almost always tested against a placebo preparation in clinical trials as a way of assessing the efficacy of a drug before it is marketed. The placebo is made to look identical to the active preparation, and the volunteers are not told whether they have been given the active drug or the placebo. Sometimes the doctor is also unaware of which preparation an individual has been given. This is known as a double-blind trial. In this way, the purely placebo effect can be eliminated and the effectiveness of the drug determined more realistically.

Sometimes just taking a medicine has a psychological effect that produces a beneficial physical response. This type of placebo response can make an important contribution to the overall effectiveness of a chemically active drug. It is most commonly seen with analgesics, antidepressants, and anti-anxiety drugs. Some people, known as placebo responders, are more likely to experience this sort of effect than the rest of the population.

DRUG INTERACTIONS

When two different drugs are taken together, or when a drug is taken in combination with certain foods or with alcohol, this may produce effects different from those produced when the drug is taken alone. Often, this is beneficial and doctors frequently make use of interactions to increase the effectiveness of a treatment. Very often, more than one drug may be prescribed to treat cancer or high blood pressure (hypertension).

Other interactions, however, are unwanted and may be harmful. They may occur not only between prescription drugs, but also between prescription and over-the-counter drugs. It is important to read warnings on drug labels and tell your doctor if you are taking any preparations – both prescription and over-the-counter, and even herbal or homeopathic remedies.

A drug may interact with another drug or with food or alcohol for a number of reasons (see below).

EXAMPLES OF IMPORTANT INTERACTIONS

Adverse interactions between drugs may vary from a simple blocking of a drug's beneficial effect to a serious reaction between two drugs that may be life-threatening. Some of the more serious adverse interactions occur between the following:

Drugs that depress the central nervous system (opioids, most antihistamines, sleeping drugs, and alcohol). The effects of two or more of these drugs together may be additive, causing dangerous oversedation.

Drugs that lower blood sugar levels and such drugs as sulphonamides and alcohol. The drug interaction increases the effect of blood-sugar-lowering drugs, thus further depressing blood sugar levels.

Oral anticoagulants and other drugs, particularly aspirin and antibiotics. As these drugs may increase the tendency to bleed, it is essential to check the effects in every case.

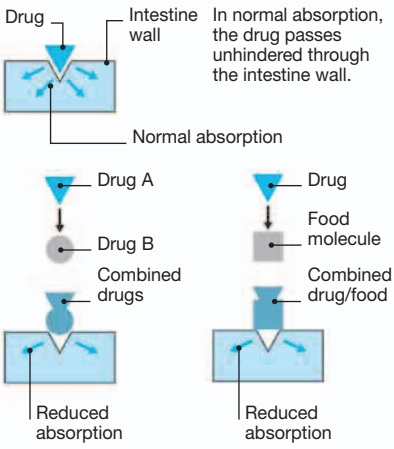
Monoamine oxidase inhibitors (MAOIs). Many drugs and foods can produce a severe increase in blood pressure when taken with MAOIs. Such drugs include amphetamines and decongestants; foods include cheese, herring, chocolate, red wine, and beer. Some of the newer MAOIs, however, are much less likely to interact with food and drugs.

Altered absorption

Alcohol and some drugs (particularly opioids and drugs with an anticholinergic effect) slow the digestive process that empties the stomach contents into the intestine. This may delay the absorption, and therefore the effect, of another drug. Other drugs (for example, metoclopramide, an anti-emetic drug) may speed the rate at which the stomach empties and may, therefore, increase the rate at which another drug is absorbed and takes effect.

Some drugs also combine with another drug or food in the intestine to form a compound that is not absorbed as readily. This occurs when tetracycline and iron tablets or antacids are taken together. Milk and dairy products also reduce the absorption of tetracycline and some other drugs, such as ciprofloxacin, by combining with the drugs in this manner.

Drug absorption in the intestine



Absorption of drug (A) may be reduced if it combines with another drug (B).

Absorption of a drug may be reduced if it combines with a food molecule.

Enzyme effects

Some drugs increase the production of enzymes in the liver that break down drugs, while others inhibit or reduce enzyme production. Thus they affect the rate at which other drugs are activated or inactivated.

Excretion in the urine

A drug may reduce the kidneys' ability to excrete another drug, raising the drug level in the blood and increasing its effect.

Receptor effects

Drugs that act on the same receptor sites (p.14) sometimes add to each other's effect on the body, or compete with each other in occupying certain receptor sites. For example, naloxone blocks receptors used by opioid drugs, thereby helping to reverse the effects of opioid poisoning.

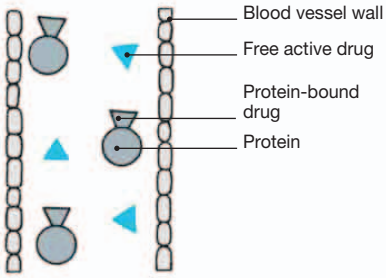
Similar or opposite effects

Drugs that produce similar effects (but act on different receptors) add to each others' actions. Often, lower doses are possible as a result, with fewer adverse effects. This is common practice in the treatment of high blood pressure and cancer. Antibiotics are given together as the infecting organisms are less likely to develop resistance to the drugs. Drugs with antagonistic effects reduce the useful activity of one or both drugs. For example, some antidepressants oppose the effects of anticonvulsants.

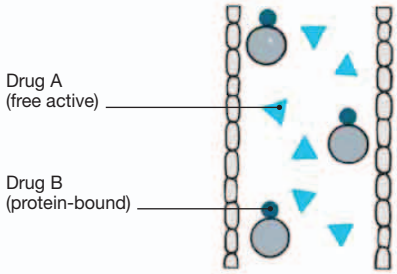
Reduced protein binding

Some drugs circulate around the body in the bloodstream with a proportion of the drug attached to the proteins of the blood plasma. The amount of drug attached to the plasma proteins is inactive. If another drug is taken, some of the second drug may also bind to the plasma proteins and displace the first drug; more of the first drug is then active in the body.

Interaction between protein-bound drugs



Protein-bound drug taken alone
Drug molecules that are bound to proteins in the blood are unable to pass into body tissues. Only free drug molecules are active.



Taken with another protein-bound drug
If a drug (B) with a greater ability to bind with proteins is also taken, drug (A) is displaced, increasing the amount of active drug.

METHODS OF ADMINISTRATION

The majority of drugs must be absorbed into the bloodstream in order for them to reach the site where their effects are needed. The method of administering a drug determines the route it takes to get into the bloodstream and the speed at which it is absorbed into the blood.

When a drug is meant to enter the bloodstream it is usually administered in one of the following ways: through the mouth or rectum, by injection, or by inhalation. Drugs that are implanted under the skin or enclosed in a skin patch also enter the bloodstream. These types are discussed under Slow-release preparations (p.18).

When it is unnecessary or undesirable for a drug to enter the bloodstream in large amounts, it may be applied topically so that its effect is limited mainly to the site of the disorder, such as the surface of the skin or mucous membranes (the membranes of the nose, eyes, ears, vagina, or rectum). Drugs are administered topically in a variety of preparations, including creams, sprays, drops, and suppositories. Most inhaled drugs also have a local effect on the respiratory tract.

Very often, a particular drug may be available in different forms. Many drugs are available both as tablets and injectable fluid. The choice between a tablet and an injection depends on a number of factors, including the severity of the illness, the urgency with which the drug effect is needed, the part of the body requiring treatment, and the patient's general state of health, in particular his or her ability to swallow.

The various administration routes are discussed in greater detail below. For a description of the different forms in which drugs are given, see Drug forms (p.19).

ADMINISTRATION BY MOUTH

Giving drugs by mouth is the most common method of administration. Most of the drugs that are given by mouth are absorbed into the bloodstream through the walls of the intestine. The speed at which the drug is absorbed and the amount of active drug that is available for use depend on several factors, including the form in which the drug is given (for example, as a tablet or a liquid) and whether it is taken with food or on an empty stomach. If a drug is taken when the stomach is empty (before meals, for example) it may act more quickly than a drug that is taken after a meal when the stomach is full.

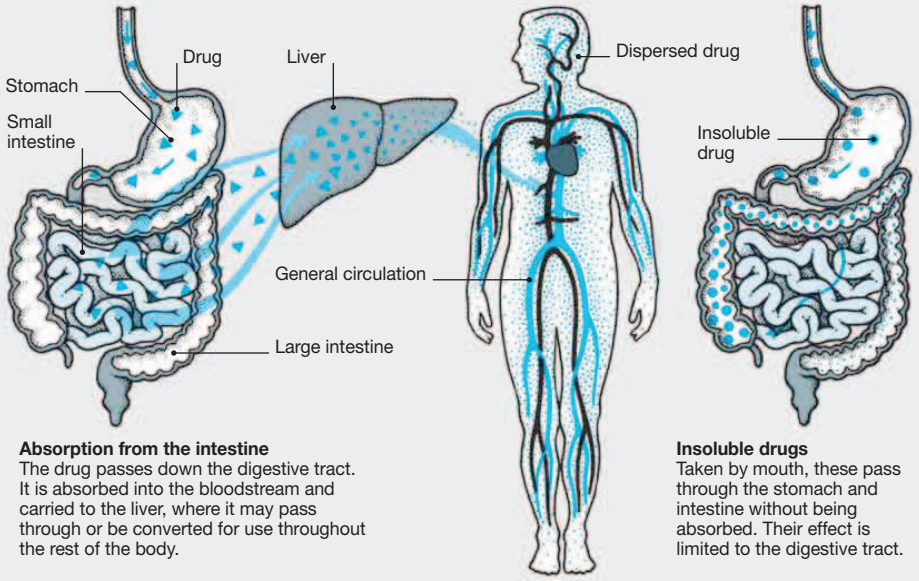
Some drugs (like antacids, which neutralize stomach acidity) are taken by mouth to produce a direct effect on the stomach or digestive tract.

In-mouth administration
Products are available that are placed in the mouth but not swallowed. They are absorbed quickly into the bloodstream through the lining of the mouth, which has a rich supply of blood vessels. Sublingual tablets are placed under the tongue, wafers are placed on the tongue, and buccal tablets are placed in the pouch between the cheek and teeth.

HOW DRUGS PASS THROUGH THE BODY

Most drugs taken by mouth reach the bloodstream by absorption through the wall of the small intestine. Blood vessels supplying the intestine then carry the drug to the liver, where it may be broken down into a form that can be used by the body. The drug (or its breakdown product) then enters the general circulation, which carries it around the body. It may pass back into the intestine before being reabsorbed into the bloodstream. Some drugs are rapidly excreted via the kidneys; others may build up in fatty tissues in the body.

Certain insoluble drugs cannot be absorbed through the intestinal wall and pass through the digestive tract unchanged. These drugs are useful for treating bowel disorders, but if they are intended to have systemic effects elsewhere they must be given by intravenous injection.



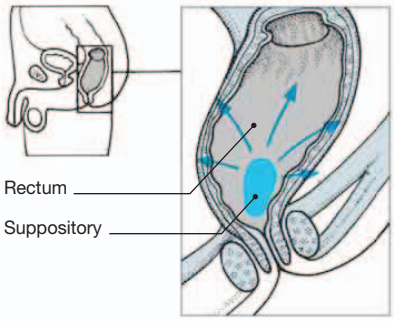
Absorption from the intestine
The drug passes down the digestive tract. It is absorbed into the bloodstream and carried to the liver, where it may pass through or be converted for use throughout the rest of the body.

Insoluble drugs
Taken by mouth, these pass through the stomach and intestine without being absorbed. Their effect is limited to the digestive tract.

RECTAL ADMINISTRATION

Drugs intended to have a systemic effect may be given in the form of suppositories inserted into the rectum, from where they are absorbed into the bloodstream. This method may be used to give drugs that might be destroyed by the stomach's digestive juices. It is also sometimes used to administer drugs to people who cannot take medication by mouth, such as those who are suffering from nausea and vomiting.

Drugs may also be given rectally for local effect, either as suppositories (to relieve haemorrhoids) or as enemas (for ulcerative colitis).



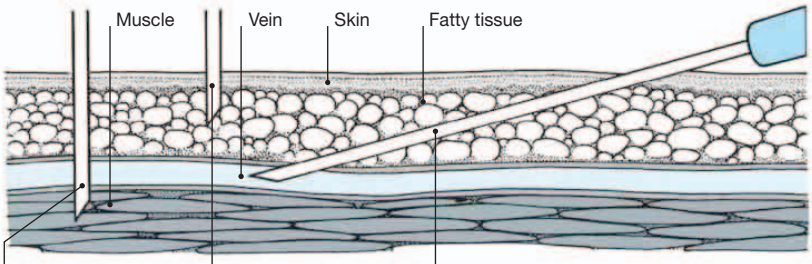
INHALATION

Drugs may be inhaled to produce a systemic effect or a direct local effect on the respiratory tract. Insufflation into the nose ("snorting") is a variation of this delivery method. Gases to produce general anaesthesia are administered by inhalation and are absorbed into the bloodstream through the lungs, producing a general effect on the body, particularly the brain. Bronchodilators (for certain types of emphysema, bronchitis, and asthma) are taken by inhalation for their direct effect on the respiratory tract, but some of the active drug also reaches the bloodstream. (See also p.48.)

ADMINISTRATION BY INJECTION

Drugs may be injected into the body to produce a systemic effect. One reason for injecting drugs is the rapid response that follows. Other circumstances that call for injection are when: a person is intolerant to the drug when taken by mouth; the drug would be destroyed by the stomach's digestive juices (insulin, for example); or the drug cannot pass through the intestinal walls into the bloodstream. Drug injections may also be given to produce a local effect, as is often done to relieve the pain of arthritis.

The three most common methods of injection – intramuscular, intravenous, and subcutaneous – are described in the illustration (see right). The type of injection depends both on the nature of the drug and the condition being treated.



Intramuscular (IM) injection
The drug is injected into a muscle, usually of the thigh, the upper arm, or the buttock.

Subcutaneous (SC) injection
The drug is injected directly under the surface of the skin.

Intravenous (IV) injection
The drug is injected directly into a vein and therefore directly into the bloodstream. Drugs given by this route act more quickly than drugs given by other types of injection.

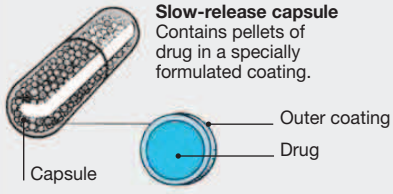
TOPICAL APPLICATION

In treating localized disorders such as skin infections and nasal congestion, it is often preferable when a choice is available to prescribe drugs in a form that has a topical, or localized, rather than a systemic effect. The reason is that it is much easier to control the effects of drugs administered locally and to ensure that they produce the maximum benefit with minimum adverse effects.

Topical preparations are available in a variety of forms, from skin creams, gels, ointments, and lotions to nasal sprays, ear and eye drops, bladder irrigations, and vaginal pessaries. It is important when using topical preparations to follow instructions carefully, avoiding a higher dose than recommended or application for longer than necessary. This will help to avoid adverse systemic effects caused by the absorption of larger amounts into the bloodstream.

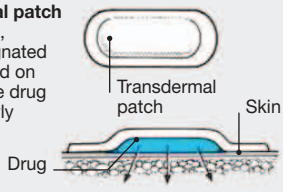
SLOW-RELEASE AND MODIFIED-RELEASE PREPARATIONS

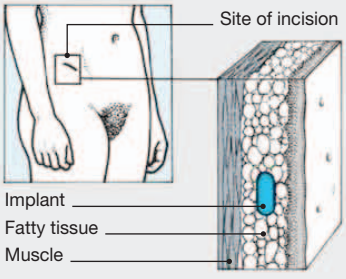
Some disorders can be treated with specially formulated preparations that can release the active drug slowly. Such preparations may be beneficial when it is inconvenient for a person to visit the doctor regularly, or when only small amounts of the drug need to be released into the body. Slow release of drugs can be achieved by depot injections, transdermal patches, capsules and tablets, and implants. Modified-release tablets and capsules are a more advanced version in which release of the active ingredient is related to time.



Slow-release capsule
Contains pellets of drug in a specially formulated coating.

Transdermal patch
An adhesive, drug-impregnated pad is placed on the skin. The drug passes slowly through the skin.





Implants
A pellet containing the drug is implanted under the skin. By this rarely used method, a drug (usually a hormone) is slowly released into the bloodstream over a period of months.

DRUG FORMS

Most drugs are specially prepared in a form designed for convenience of administration. This helps to ensure that dosages are accurate and that taking the medication is as easy as possible. Inactive ingredients (those with no therapeutic effect) are sometimes added to flavour or colour the medicine, or to improve its chemical stability, extending the period during which it is effective. The more common drug forms are described below.

Tablets

These contain the drug compressed with other ingredients (see right) into a solid plug. Tablets can be either coated with a membrane that allows the drug to be released slowly for sustained effect or made up of individually layered granules for slow release; they can also be soluble in water.

Capsules

The drug is contained in a cylindrically shaped gelatin shell that breaks open after the capsule has been swallowed, releasing the drug. Slow-release capsules contain pellets that dissolve in the gastrointestinal tract, releasing the drug slowly (facing page).

Wafers/melts, pastilles, or lozenges

The drug is contained in a small wafer (or melt) placed on the tongue and allowed to dissolve. A pastille is a medicated "sweet" that is chewed; a lozenge is sucked.

Liquids (oral)

Some drugs are available as liquid; the active substance is combined in a solution, suspension, or emulsion with preservatives, solvents, and flavouring or colouring agents. Many liquid preparations should be shaken before use, to ensure even distribution of the active drug, or inaccurate dosages may result.

Mixture

A mixture is one or more drugs, either dissolved to form a solution or suspended in a liquid (often water).

Elixir

An elixir is a solution of a drug in a sweetened mixture of alcohol and water. It is often highly flavoured.

Emulsion

An emulsion is a drug dispersed in oil and water. An emulsifying agent is often included to stabilize the product.

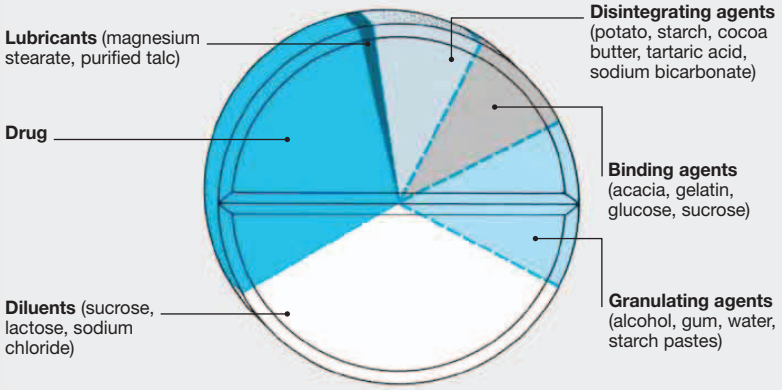
Syrup

A syrup is a concentrated solution of sugar containing the active drug, with flavouring and stabilizing agents added.

Topical skin preparations

These are designed for application to the skin and other surface body tissues.

WHAT A TABLET CONTAINS


Lubricants (magnesium stearate, purified talc)
Drug
Diluents (sucrose, lactose, sodium chloride)
Disintegrating agents (potato, starch, cocoa butter, tartaric acid, sodium bicarbonate)
Binding agents (acacia, gelatin, glucose, sucrose)
Granulating agents (alcohol, gum, water, starch pastes)

Diluents add bulk. Binders and granulating agents bind the ingredients. Lubricants ensure a smooth surface by allowing the ingredients to flow during the manufacturing process.

Disintegrating agents help the tablet dissolve. A sugar coating or a transparent film protects the surface or modifies the drug's release rate. Dyes and imprints make it recognizable.

Preservatives are usually included to reduce bacterial growth. The most commonly used skin preparations are described below. (See also Bases for skin preparations, p.135.)

Creams, ointments, and gels

A cream is a non-greasy preparation that is used to apply drugs to an area of the body or to cool or moisten the skin. It is less noticeable than an ointment.

An ointment is a greasy preparation used to apply drugs to an area of the body, or as a protective or lubricant layer for the relief of dry skin conditions.

A gel is a jelly-like suspension consisting of small, insoluble particles dispersed through a liquid. Most gels are non-greasy. They are most commonly used for face and scalp preparations.

Lotion

A lotion is a solution or suspension applied to unbroken skin to cool and dry the affected area. Some are more suitable for use in hairy areas because they are not as sticky as creams or ointments.

Injection solutions

Solutions for injections are sterile (germ-free) preparations of a drug dissolved or suspended in a liquid. Other chemicals (e.g., anti-oxidants and buffers) are often added to preserve the stability of the drug or to regulate the acidity or alkalinity of the solution. Most injectable drugs are packaged in sterile, disposable syringes. For details on different types, see Administration by injection, facing page.

Suppositories and pessaries

These are solid, bullet-shaped dosage forms designed for easy insertion into the rectum (suppository) or vagina (pessary). They contain a drug and an inert (chemically and pharmacologically inactive) substance often derived from vegetable oil or cocoa butter. The drug is gradually released in the rectum or vagina as the suppository or pessary dissolves at body temperature.

Eye drops

A sterile drug solution (or suspension) dropped behind the eyelid.

Ear drops

A solution (or suspension) containing a drug introduced into the ear by dropper. Ear drops are usually given to produce an effect on the outer ear canal.

Nasal drops/spray

A solution of a drug for introduction into the nose to produce a local effect.

Inhalers

Aerosol inhalers contain a solution or suspension of a drug under pressure. Dry-powder devices contain the drug in an inhalable powder form. A valve ensures delivery of a recommended dosage when the inhaler is activated. A mouthpiece facilitates inhalation as the drug is released from the canister. It is important to use the correct technique; you should follow the printed instructions carefully or ask your doctor, pharmacist, or nurse to show you what to do. Aerosol and dry-powder inhalers are widely used for asthma. (See also p.49.)

Transdermal patches

These adhesive pads are impregnated with a drug and placed on the skin. The drug is released slowly through the skin (facing page).

DRUG TREATMENT IN SPECIAL RISK GROUPS

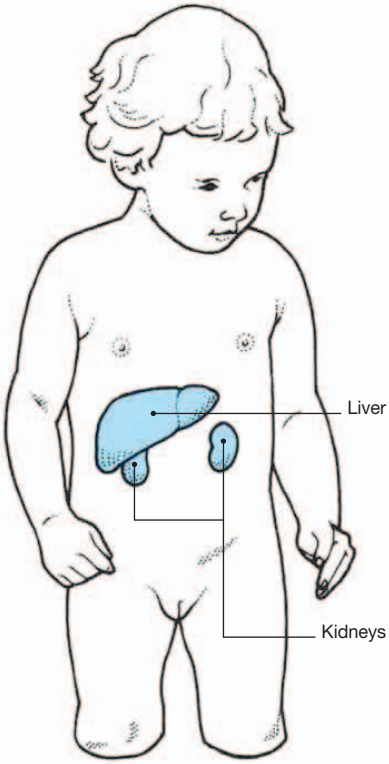
Different people tend to respond in different ways to drug treatment. Taking the same drug, one person may suffer adverse effects while another does not. However, doctors know that certain people are always more at risk from adverse effects when they take drugs; the reason is that in those people the body handles drugs differently, or the drug has an atypical effect. Those people at special risk include infants and children, women who are pregnant or breast-feeding, the elderly, and people with long-term medical conditions, especially those who have impaired liver or kidney function.

The reasons that such people may be more likely to suffer adverse effects are discussed in detail on the following pages. Others who may need special attention include those already taking regular medication who may risk complications when they take another drug. Drug interactions are discussed more fully on p.16.

When doctors prescribe drugs for people at special risk, they take extra care to select appropriate medication, adjust dosages, and closely monitor the effects of treatment. If you think you may be at special risk, be sure to tell your doctor in case he or she is not fully aware of your particular circumstances. Similarly, if you are buying over-the-counter drugs, you should ask your doctor or pharmacist if you think you may be at risk of experiencing any possible adverse effects or hazardous drug interactions.

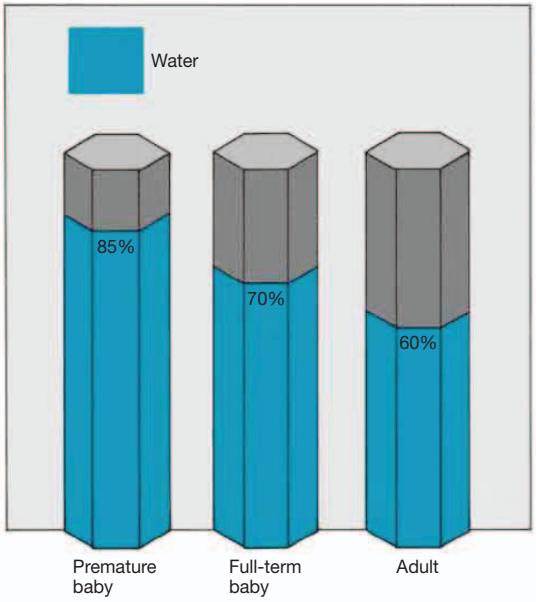
INFANTS AND CHILDREN

Infants and children need a lower dosage of drugs than adults because children have a relatively low body weight. In addition, because of differences in body composition and the distribution and amount of body fat, as well as differences in the state of development and function of organs such as the liver and kidneys at different ages, children cannot simply be given a proportion of an adult dose as if they were small adults. Dosages need to be calculated in a more complex way, taking into account the child's age and weight. While newborn babies often have to be given very small doses of drugs, older children may need relatively large doses of some drugs compared to the adult dosage.



The liver
The liver's enzyme systems are not fully developed when a baby is born. This means that drugs are not broken down as rapidly as in an adult, and may reach dangerously high concentrations in the baby's body. For this reason, many drugs are not prescribed for babies or are given in very reduced doses. In older children, because the liver is relatively large compared to the rest of the body, some drugs may need to be given in proportionately higher doses.

The kidneys
During the first six months, a baby's kidneys are unable to excrete drugs as efficiently as an adult's kidneys. This may lead to a dangerously high concentration of a drug in the blood. The dose of certain drugs may therefore need to be reduced. Between one and two years of age, kidney function improves, and higher doses of some drugs may then be needed.



Body composition
The proportion of water in the body of a premature baby is about 85 per cent of its body weight, that of a full-term baby is 70 per cent, and that of an adult is only 60 per cent. This means that drugs that stay in the body water will not be as concentrated in an infant's body as in an adult's, unless a higher dose relative to body weight is given.

PREGNANT WOMEN

Great care is needed during pregnancy to protect the fetus so that it develops into a healthy baby. Drugs taken by the mother can cross the placenta and enter the baby's bloodstream. With certain drugs, and at certain stages of pregnancy, there is a risk of developmental abnormalities, retarded growth, or post-delivery problems affecting the newborn baby. In addition, some drugs may affect the health of the mother during pregnancy.

Many drugs are known to have adverse effects during pregnancy; others are known to be safe, but in a large number of cases there is no firm evidence to decide on risk or safety. Therefore, the most important rule if you are pregnant or trying to conceive is to consult your doctor before taking any prescribed or over-the-counter medication.

Drugs such as cannabis, nicotine, and alcohol should also be avoided during pregnancy. A high daily intake of caffeine should be reduced if possible. Your doctor will assess the potential benefits of drug treatment against any possible risks to decide whether or not a drug should be taken. This is particularly important if you need to take medication regularly for a chronic condition such as epilepsy, high blood pressure, or diabetes.

Drugs and the stages of pregnancy

Pregnancy is divided into three three-month stages called trimesters. Depending on the trimester in which they are taken, drugs can have different effects on the mother, the fetus, or both. Some drugs may be considered safe during one trimester, but not during another. Doctors, therefore, often need to substitute one medication for another given during the course of pregnancy and/or labour.

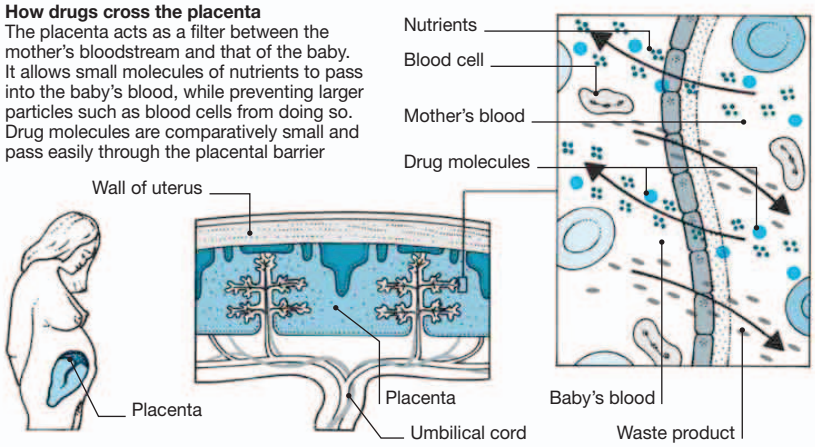
The trimesters of pregnancy

First trimester
During the first three months of pregnancy – the most critical period – drugs may affect the development of fetal organs, leading to congenital malformations. Very severe defects may result in miscarriage.

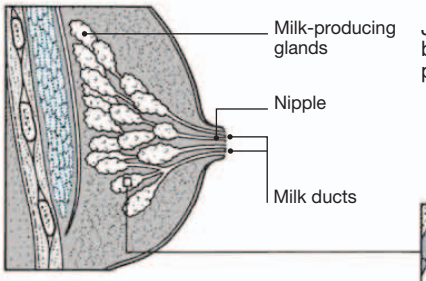
Second trimester
From the fourth to the sixth month some drugs may retard the growth of the fetus. This may also result in a low birth weight. Other drugs may affect the development of the nervous system.

Third trimester
During the last three months of pregnancy, major risks include breathing difficulties in the newborn baby. Some drugs may also affect labour, causing it to be premature, delayed, or prolonged.

How drugs cross the placenta
The placenta acts as a filter between the mother's bloodstream and that of the baby. It allows small molecules of nutrients to pass into the baby's blood, while preventing larger particles such as blood cells from doing so. Drug molecules are comparatively small and pass easily through the placental barrier

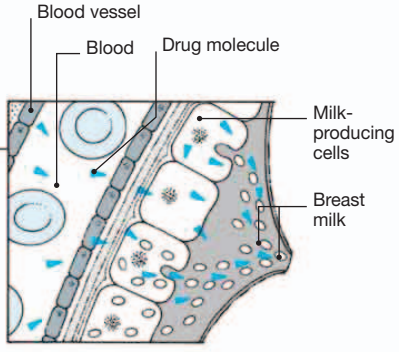


BREAST-FEEDING



How drugs pass into breast milk
The milk-producing glands in the breast are surrounded by a network of fine blood vessels. Small molecules of substances such as drugs pass from the blood into the milk. Drugs that dissolve easily in fat may pass across in greater concentrations than other drugs.

Just as drugs may cross from the mother's bloodstream into the baby's through the placenta, they may also pass to the baby from the mother's milk. This means that a breast-fed baby will receive small doses of whatever drugs the mother is taking. In many cases this is not a problem, because the amount of drug that passes into the milk is too small to have any significant effect on the baby. However, some drugs can produce unwanted effects on the baby. Antibiotics may sensitize the infant and consequently prevent their use later in life. Sedative drugs may make the baby drowsy and cause feeding problems. Moreover, some drugs may reduce the amount of milk produced by the mother.



Doctors usually advise breast-feeding women to take only essential drugs. When a mother needs to take regular medication while breast-feeding, her baby may also need to be closely monitored for possible adverse effects.

THE ELDERLY

Older people are particularly at risk when taking drugs. This is partly due to the physical changes associated with ageing, and partly because many elderly people need to take several different drugs at the same time. They may also be at risk because they may be unable to manage their treatment properly, or they may lack the information to do so.

Physical changes

Elderly people have a greater risk of accumulating drugs in their body tissues because the liver is less efficient at breaking drugs down and the kidneys are less efficient at excreting them. Because of this, in some cases the normal adult dose will produce side effects, and a smaller dose may be needed to produce a therapeutic effect without the side effects. (See also Liver and kidney disease, below.)

Older people tend to take more drugs than younger people – many take three or more drugs at the same time. Apart from increasing the number of drugs in their systems, adverse drug interactions (see p.16) are more likely.

As people grow older, some parts of the body, such as the brain and nervous system, may become more sensitive to drugs, thus increasing the likelihood of adverse reactions from drugs acting on those sites (see right). A similar problem may occur due to changes in the percentage of body fat. Although allergic reactions (see Allergy, p.81) do not become commoner due to increasing age, they are more likely because more drugs are prescribed. Accordingly, doctors prescribe more carefully for older people, especially those with disorders that are likely to correct themselves in time.

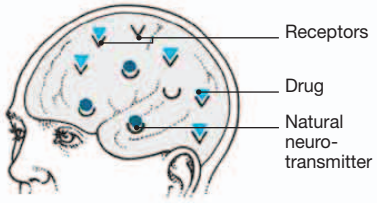
Incorrect use of drugs

Elderly people often suffer harmful effects from their drug treatment because they fail to take their medication regularly or correctly. This may happen because they have been misinformed about how to take it or receive vague instructions. Problems arise sometimes because the elderly person cannot remember whether he or she has taken the drug and takes a double dose (see Exceeding the dose, p.30). Problems may also occur because the person is confused; this is not necessarily due to age or illness, but can arise as a result of drug treatment, especially if an elderly person is taking a number of different drugs or a sedative.

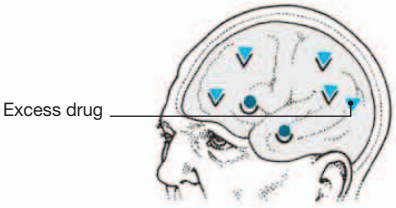
Prescriptions for the elderly should be clearly and fully labelled, and/or information about the drug and its use should be provided either for the individual or for the person taking care of him or her. When appropriate, containers with memory aids should be used to dispense the medication in single doses.

Elderly people often find it difficult to swallow medicine in capsule or tablet form; they should always take capsules or tablets with a full glass or cup of liquid. A liquid medicine may be prescribed instead.

Effect of drugs that act on the brain



In young people
There are plenty of receptors to take up the drug as well as natural neurotransmitters.



In older people
There may be fewer receptors so that even a reduced drug dose may be excessive.

LIVER AND KIDNEY DISEASE

Long-term illness affects the way in which people respond to drugs. This is especially true of liver and kidney problems. The liver alters the chemical structure of many drugs that enter the body (see How drugs pass through the body, p.17) by breaking them down into simpler substances, while the kidneys excrete drugs in the urine. If the effectiveness of the liver or kidneys is reduced by illness, the action of drugs on the individual can be significantly altered. In most cases, people with liver or kidney disease will be prescribed a smaller number of drugs and lower doses. In addition, certain drugs may, in rare cases, damage the liver or kidneys. For example, tetracycline can cause kidney failure in those with poor kidney function. A doctor may be reluctant to prescribe such a drug to someone with already reduced liver or kidney function in order to avoid the risk of further damage.

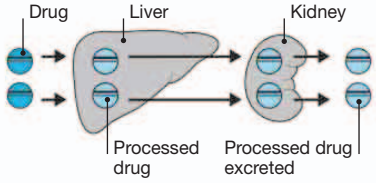
Drugs and liver disease

Severe liver diseases, such as cirrhosis and hepatitis, affect the way the body breaks down drugs. This can lead to a dangerous accumulation of certain drugs in the body. People suffering from these diseases should consult their doctor before taking any medication (including over-the-counter drugs) or alcohol. Many drugs must be avoided completely, since they could cause coma in someone with liver damage.

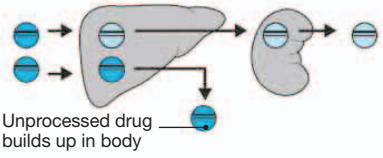
Drugs and kidney disease

People with poor kidney function are at risk from drug side effects. There are two reasons for this. First, drugs build up in the system because smaller amounts are excreted in urine. Second, kidney disease can cause protein loss through the urine, which lowers the level of protein in the blood. Some drugs bind to blood proteins, and if there are fewer protein molecules, a greater proportion of drug becomes free and active in the body.

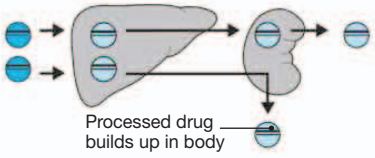
Drug passing through body



Normal liver and kidneys
Drugs are processed in the liver before being excreted by the kidneys.



In liver damage
The liver cannot process sufficient drug and this builds up in the body tissues.



In kidney damage
The kidneys cannot excrete the processed drug in the urine and drug levels in the body rise.

DRUG TOLERANCE AND DEPENDENCE

In the course of treatment with some common drugs, the body acquires the ability to adapt to the drug's effect. This response is known as tolerance. As a result, the drug dose has to be increased to achieve the same effect as before. Tolerance is not always associated with dependence (often called addiction), which is the compulsion to continue taking a drug in order to experience a desired effect, or in order to avoid the unpleasant effects that occur when it is not taken. Dependence is almost always confined to drugs which act on the brain and nervous system, such as opiates, tobacco, and alcohol.

TOLERANCE

Drug tolerance occurs as the body adapts to a drug's actions. A person taking the drug needs larger and larger doses to achieve the original effect and as the dose increases, so too do the risks of toxic effects and dependence. Although people can develop a tolerance to some drugs, it is an important characteristic of virtually all the drugs of dependence.

How tolerance develops

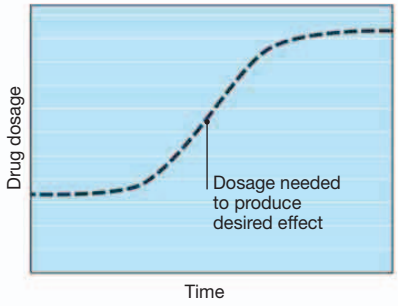
Drug tolerance can develop through a variety of different mechanisms, many of which are not fully understood. In some cases, the liver becomes more efficient at breaking the drug down to an inactive form. In other cases, the drug receptors adapt to the presence of the drug, In yet other cases, the drug exhausts the body's supply of chemicals necessary to produce a response.

Tolerance to one particular drug may result in the reduced effect of a drug that has similar properties or is processed in the body in the same way. This is known as cross tolerance. For example, a regular drinker, who can tolerate high levels of alcohol (a depressant), can have a dangerous tolerance to other depressants such as sleeping drugs and anti-anxiety drugs. While cross-tolerance can often cause problems, it sometimes has a beneficial effect in allowing a substance with a less addictive potential to replace the original drug. For example, the symptoms of alcohol withdrawal can be controlled by the anti-anxiety drug diazepam, which is also a depressant.

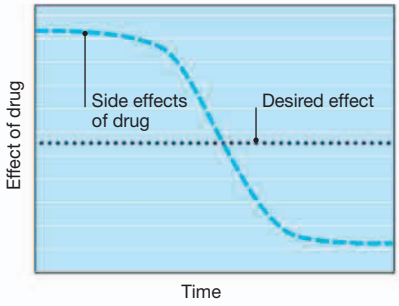
Tolerance to some drugs has its benefits. A person can develop tolerance to the side effects of a drug while still benefiting from its useful effects. For example, many people taking antidepressants find that side effects such as dry mouth slowly disappear, with the primary action of the drug continuing (see below).

Increasing drug tolerance has dangers. A person who has developed tolerance to a drug may keep raising the dose to sometimes toxic levels in order to achieve the desired effect.

Effects of tolerance



Development of tolerance
A gradually increasing dose of the drug is needed to produce the desired effect as tolerance develops over time.



Beneficial effect of tolerance
During treatment with many drugs, the unwanted side effects decrease with time, while the desired effect of the drug is maintained.

DEPENDENCE

Drug dependence is defined as the compulsive use of a substance resulting in physical, psychological, or social harm to the user, with continued use despite the harm.

Drug dependence (now widely preferred as a term to the word addiction) applies far more widely than most people realize. It is usually thought of in association with the use of illegal drugs, such as heroin, or with excessive intake of alcohol. But millions of people are dependent on other drugs, including stimulants – such as caffeine found in coffee and tea, and nicotine in tobacco – and certain prescription medicines, such as analgesics, sleeping drugs, amphetamines, and tranquillizers.

Psychological and physical dependence

Drug dependence, implying that a person is reliant on the continued use of a substance with potential for abuse, is of two types. Psychological dependence is an emotional state of craving for a drug whose presence has a desired effect on the mind, or whose absence has an undesired effect. Physical dependence, which often accompanies psychological dependence, involves physiological adaptation to a medicine or alcohol that is characterized by severe physical disturbances – withdrawal symptoms – during a period of abstinence. Some drugs, such as laxatives, can produce physical dependence.

Drugs that cause dependence

Many people who need to take regular medication worry that they may become dependent on their drugs. In fact, only a few groups of drugs produce physical or psychological dependence, and most of them are substances that alter mood or behaviour. Such drugs include heroin and other opioid analgesics such as morphine and pethidine, sleeping and anti-anxiety drugs (benzodiazepines and barbiturates), depressants (alcohol), and nervous system stimulants (cocaine, caffeine, amphetamines, and nicotine).

Antidepressant drugs do not cause psychological dependence. When a depressive illness has been treated effectively, drugs can usually be stopped

DEPENDENCE continued

without any problems, although some people may experience physical withdrawal symptoms if drugs are stopped suddenly. Consult the drug profile in Part 3 of this book to discover the dependence rating of any drug you are taking.

The use of nicotine, in the form of tobacco, and of opioid analgesics, whether controlled or uncontrolled, invariably produces physical dependence if occurring regularly over a period of time. However, it is also true that not all regular users of alcohol become alcoholics. There is much argument over the definition of an alcoholic. A widely used definition is: a person who has experienced physical, psychological, social, or occupational impairment as a consequence of habitual, excessive consumption of alcohol.

Recognizing the dangers of drug dependence

Factors that determine a person's risk of developing physical dependence include the characteristics of the drug itself, the strength and frequency of doses, and the duration of use. However, the presence of these factors does not always result in dependence. Psychological and physiological factors that are unique to each individual also enter into the equation, and there may be other, as yet unknown, factors involved. For example, when the use of opioid analgesics is restricted to the short-term relief of pain in a medical setting, dependence is rare. Yet there is a high risk of physical dependence when opioid analgesics, or other drugs of abuse, are taken for non-medical reasons. There is also a risk in some cases of low-dose use when the drug is continued over a long period (e.g. with benzodiazepines, p.39). No one can say for sure exactly what leads a person to drug-dependent behaviour. A person's psychological and physical make-up are thought to be factors, as well as his or her social environment, occupational pressures, and outlook on life.

The indiscriminate use of certain prescription drugs can also cause drug dependence. Benzodiazepine drugs can produce dependence, and this is one reason why doctors today discourage the use of any drug to induce sleep or calm anxiety for more than a few weeks. Appetite suppressants (see p.44) require close medical supervision. Amphetamines are no longer prescribed as appetite suppressants because of the frequency with which they are abused.

Treating drug dependence

Treatment for drug dependence can only be effective if the person is sufficiently motivated. There are two parts to treatment. The first part, detoxification, can take different forms. In some cases, if it is possible to do so, abstinence may be abruptly imposed. Sometimes, the drug may be gradually withdrawn or other safer substances substituted. For example, methadone (p.313) is substituted for heroin. Physical or mental withdrawal symptoms may need close monitoring, for instance, withdrawal from depressants such as barbiturates or alcohol may result in seizures. Once the drug has been cleared from the body, the second part of treatment is directed at preventing a recurrence. This can involve psychological therapies to tackle the initial cause of the dependence, such as social problems or depression. Psychotherapy, personal counselling, and the work of support organizations, such as Alcoholics Anonymous, may all play a role in the rehabilitation of the alcoholic or addict.

DRUG MISUSE

The term is defined as any use of drugs that causes physical, psychological, economic, legal, or social harm to the user, or to persons who may be affected by the user's behaviour. Drug abuse commonly refers to taking drugs obtained illegally (such as heroin), but may also be used to describe the misuse of drugs generally obtainable legally (nicotine, alcohol), and to drugs obtainable through a doctor's prescription only (everything from sleeping tablets and tranquillizers to analgesics and stimulants).

The misuse of prescription drugs deserves more attention than it usually receives. The practice can include the personal use of drugs left over from a previous course of treatment, the sharing with others of drugs that have been prescribed for yourself, the deliberate deception of doctors, the forgery of prescriptions, and the theft of drugs from pharmacies. All of these practices can have dangerous consequences. Careful attention to the advice in the section on Managing your drug treatment (p.25) will help to avoid inadvertent misuse of drugs. The dangers associated with abuse of individual drugs are discussed under Drugs of abuse (pp.439–450).

Commonly misused drugs

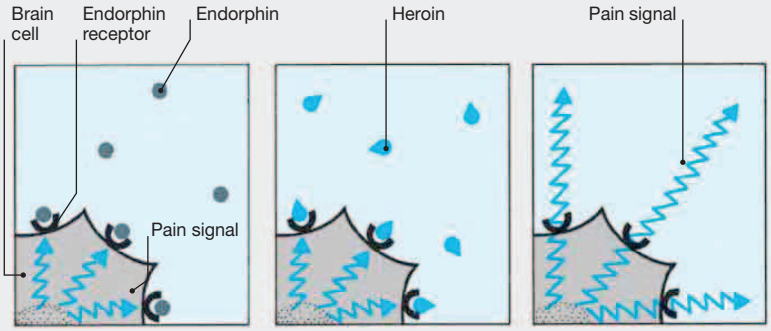
- Alcohol
- Amphetamines
- Barbiturates
- Benzodiazepines
- Cannabis
- Cocaine (including crack)
- Ecstasy (MDMA)
- GHB
- Ketamine
- Khat
- Lysergide (LSD)
- "Magic mushrooms"
- Mephedrone
- Naphyrone
- Nicotine
- Nitrites
- Opioids (including heroin and methadone)
- Phencyclidine
- Volatile substances (solvents)

SYMPTOMS OF WITHDRAWAL

These can range from the mild (sneezing, sweating) to the serious (vomiting, confusion) to the extremely serious (seizures, coma). Alcohol withdrawal may be associated with delirium tremens, very occasionally fatal. Withdrawal from benzodiazepines can sometimes involve hallucinations and seizures. But under medical guidance, withdrawal symptoms can be relieved with doses of the original drug, or with less addictive substitutes.

Withdrawal symptoms occur because the body has adapted to the action of the drug (see Drug tolerance, p.23). When a drug is continuously present, the body may stop the release of a natural chemical necessary for normal body function, such as endorphins (see illustrations below).

Pain and heroin withdrawal



Normal brain
When no drug is present, natural substances called endorphins inhibit the transmission of pain signals.

Effect of heroin
Heroin occupies the same receptors in the brain as endorphins, suppressing production of endorphins.

Heroin withdrawal
Abrupt withdrawal of heroin leaves the brain without a buffer to pain signals, even from minor stimuli.

MANAGING YOUR DRUG TREATMENT

A prescribed drug does not automatically produce a beneficial response. For a drug to have maximum benefit, it must be taken as directed by the doctor or manufacturer. It is estimated that four out of every six people for whom a drug is prescribed do not take it properly; one in six, not at all. The reasons include failure to understand or remember instructions, fear of adverse reactions, and lack of motivation, often arising from the disappearance of symptoms.

It is your responsibility to take a prescribed drug at the correct time, and as instructed. In order to do this, you need to know where to obtain information about the drug (see Questioning your prescriber, p.26) and to make certain that you fully understand the instructions.

The following pages describe the practical aspects of drug treatment, from obtaining a prescription and buying over-the-counter drugs to storing drugs and disposing of old medications safely. Problems caused by mismanaging drug treatment – overdosing, underdosing, or stopping the drug altogether – and long-term drug treatment are dealt with on pp.28–31. Information regarding specific drugs is given in Part 3.

OVER-THE-COUNTER DRUGS

Over-the-counter drugs are those for which a prescription is not required. All are available from pharmacies (many only from pharmacies) but some, called General Sales List (GSL) medicines, are very widely sold, even by supermarkets.

It is generally accepted that over-the-counter drugs are suitable for self-treatment and are unlikely to produce serious adverse reactions if taken as directed. But, as with all medicines, they can be harmful if misused. The ease with which they can be bought is no guarantee of their absolute safety. For this reason, the same precautions should be taken when using any over-the-counter medicine as when using a prescription drug.

Using over-the-counter drugs

A number of ailments and problems, ranging from coughs and colds to minor cuts and bruises, can be treated with over-the-counter medicines; and some medicines, such as antibiotic eye drops, which were once only available with a prescription, can now be bought over the counter. However, you must be sure to read and follow carefully the directions on the label, particularly the advise on dosage and the circumstances in which a doctor should be consulted. Most over-the-counter drugs are clearly labelled. They may warn of conditions under which the drug should not be taken, or advise you to consult a doctor if symptoms persist.

Your pharmacist is a good source of information about over-the-counter drugs and can usually tell you what is suitable for your complaint. He or she can also determine when an over-the-counter drug may not be effective and can warn you if self-or prolonged treatment is not advisable. When consulting the pharmacist about over-the-counter drugs, you should tell him or her if you are taking prescription drugs or treatments for any other illnesses.

BUYING MEDICINES OVER THE INTERNET

There are many websites offering over-the-counter (OTC) and prescription-only medicines (POM) for sale over the internet. Buying medicines from these sites is potentially very dangerous. Many of them operate outside the UK, so they are not subject to UK law and the drugs they sell and the advice they give are not regulated in the same way as in the UK (through the MHRA). This means the quality of the drugs they supply cannot be guaranteed. You may receive either substandard or fake drugs, with the risk that you could suffer under- or overdosing or even toxic adverse effects from taking the wrong drug or a toxic contaminant. You should be especially suspicious if the site will supply you with a POM medicine without a prescription. If the site displays the logo of the Royal Pharmaceutical Society of Great Britain (a green box containing a green cross, the words "Registered Pharmacy", and a registration number) this is more reassuring, and clicking on this logo should take you to the RPS website, which will confirm the site is that of an officially UK-registered pharmacy. These sites will only supply POM medicines if you have a prescription from a registered UK prescriber.

Buying over-the-counter medications
Various drugs, from cough medicine to antibiotic eye drops, are available over the counter. Your pharmacist can often help you to select the appropriate medication.

Medicated creams, lotions, and powders

Analgesics

Eye preparations

Laxatives

Cough and cold treatments

Antacids

It is important to speak to your doctor before buying over-the-counter drugs for children. Some symptoms, such as diarrhoea in young children, should be treated only by a doctor since they may be caused by a serious condition.

PRESCRIPTION DRUGS

Prescription-only medicines (POMs) can only be prescribed by a doctor, dentist, specially qualified nurse-prescriber, or a prescribing pharmacist. Such drugs are not necessarily "stronger" or more likely to have side effects than those you can buy without prescription. Indeed, you may be given a POM that is also available over the counter. Drugs that are available only on prescription are drugs whose safe use is difficult to ensure without medical supervision.

When you are prescribed a drug, it is usually started at the normal dosage for the disorder being treated. The dosage may later be adjusted (lowered or increased) if the drug is not producing the desired effect or if there are adverse effects, or it may even be switched to an alternative drug that may be more effective.

Prescribing generic and brand-name drugs

When writing a prescription for a drug, the prescriber often has a choice between a generic and a brand-name product. Although the active ingredient is the same, two versions of the same drug may act in slightly different ways, as each manufacturer may formulate their product differently. They may also look different. In most cases, the differences are not important for the clinical effect of the drug. Generic drugs are often cheaper than brand-name products, and their use therefore provides a substantial cost-saving to the NHS.

Community pharmacists are obliged to dispense precisely what the doctor has written on the prescription form and are not allowed to substitute a generic drug when a brand-name has been specified. However, if you are prescribed a generic drug, the pharmacist is free to dispense whatever version of this drug is available. This means that your regular medication may vary in appearance each time you renew your prescription.

Hospital pharmacies often dispense generic versions of certain drugs. Therefore, if you are in hospital, the regular medication you receive may look different from that which you are used to at home.

Your prescription

It is advisable for you to obtain all of your prescription drugs from the same pharmacist or at least from the same pharmacy, so that your pharmacist can advise you about any particular problems you may have, and keep supplies of any unusual drugs you may be taking.

If you need to take drugs that are prescribed by more than one doctor, or by your dentist in addition to your doctor, the pharmacist is able to call attention to possible harmful interactions. Doctors do ask if you are taking other medicines, but your regular pharmacist provides valuable additional advice.

Questioning your prescriber

Lack of information is the most common reason for drug failure. Comments like "The doctor is too busy to be bothered with a lot of questions" or "The doctor will think I'm stupid if I ask that" are common. Be certain you understand the instructions for a drug before you take it, and don't hesitate to ask if you have any questions about your drug treatment.

It is a good idea to make a list of the questions you may want to ask before your visit, and to make a few notes while you are there about what you are told. It is not uncommon to forget some of the instructions your prescriber gives you during a consultation.

Know what you are taking

Your prescriber should tell you the generic or brand name of the drug he or she is prescribing, and exactly what condition or symptom it has been prescribed for.

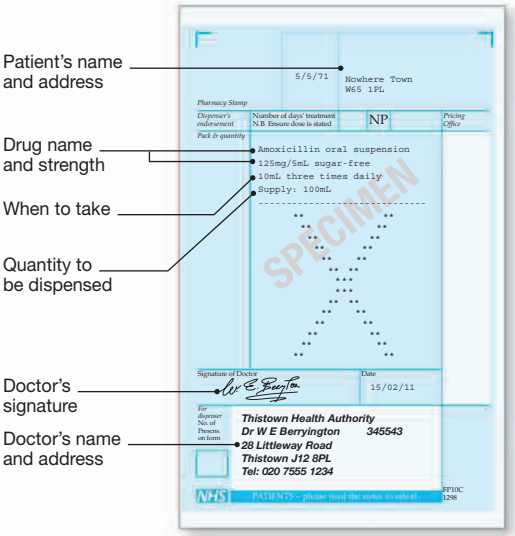
As well as telling you the name of the drug prescribed, your prescriber should explain what dose you should take, how often to take it, and whether the prescription should be repeated. Be certain you understand the instructions about how and when to take the drug (see also Taking your medication, facing page). For example, does four times a day mean four times during the time you are awake, or four times in 24 hours? Ask your prescriber how long the treatment should last; some medications cause harmful effects if you stop taking them abruptly, or do not have beneficial effects unless the course of drug treatment is completed.

To help you remember, the label on your dispensed medicine may repeat the instructions, and the pharmacist will give you a patient information leaflet that will give you detailed information about the drug. You should make sure you read this leaflet before taking your medication.

Risks and special precautions

All drugs have adverse effects (see The effects of drugs, p.15), and you should know what these are. Ask your prescriber what the possible adverse effects of the drug are and what you should do if they occur. Also ask if there are any foods, activities (such as driving), or other drugs you should avoid during treatment, and whether it is safe to drink alcohol while taking the drug.

Your prescription
Your prescription tells the pharmacist what to supply and what to put on the label. If the prescription and label differ, ask the pharmacist about it. The label may have a "do not use after" date. If it does not, ask the pharmacist to advise you. Usually, you will receive a Patient Information Leaflet, which gives details about the drug, its adverse effects, whether it is safe for you, when not to use it, and so on. Compare this with your doctor's instructions, and ask the pharmacist about any differences.



PRESCRIPTION TERMS

ac before food
ad lib freely
AM morning
bd twice a day
c with
cap capsule
cc cubic centimetre
ext for external use
gtt drops
mcg micrograms
mg milligrams
ml millilitres
nocte at night
od each day
om each morning
on each night
pc after food
PM evening
po by mouth
pr by rectum
prn as needed
pv by vagina
qds four times a day
s without
sr slow release
stat at once
tab tablet
tds three times a day
top apply topically
ud use as directed
x times

TAKING YOUR MEDICATION

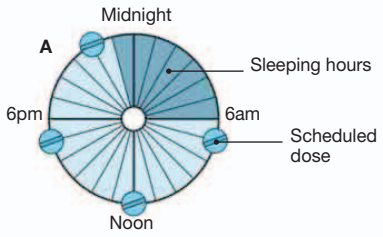
Among the most important aspects of managing your drug treatment is knowing how the drug is to be taken. Should it be taken on an empty stomach? With food? When? Mixed with something? Specific instructions on such points are given in the individual drug profiles in Part 3.

When to take your drugs

Certain drugs, such as analgesics and drugs for migraine, are taken only as necessary, when warning symptoms occur. Others are meant to be taken regularly at specified intervals. The prescription or label instructions can be confusing, however. For instance, does four times a day mean once every six hours out of 24 – at 8 am, 2 pm, 8 pm, and 2 am? Or does it mean take at four equal intervals during waking hours – morning, lunchtime, late afternoon, and bedtime? The latter is usually the case but you need to ask your doctor for precise directions.

The actual time of day that you take a drug is generally flexible, so you can normally schedule your doses to fit your daily routine. This has the added advantage of making it easier for you to remember to take your drugs. For example, if you are to take the drug three times during the day, it may be most convenient to take the first dose at 7 am, the second at 3 pm, and the third at 11 pm, while it may be more suitable for another person on the same regimen to take the first dose at 8 am, and so on. You must, however, establish with your doctor or pharmacist your whether the drug should be taken with food, in which case you would probably need to take it with your breakfast, lunch, and dinner. Try to take your dose at the recommended intervals; if you take them too close together, the risk of side effects occurring is increased.

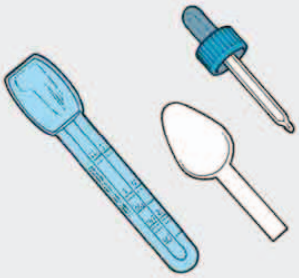
Four times a day?



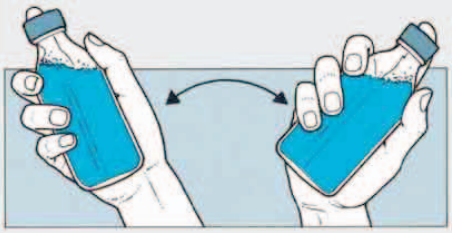
Check with your doctor whether your prescription means (A) take your drug 4 times a day during waking hours, or (B) take 4 times over a 24-hour period.

TIPS ON TAKING MEDICINES

● Whenever possible, take capsules and tablets while standing up or in an upright sitting position, and take them with water. If you take them when you are lying down, or without enough water, it is possible for the capsules or tablets to become stuck in the oesophagus. This can delay the action of the drug and may damage the oesophagus.



● Always measure your dose carefully, using a 5ml spoon or an accurate measure such as a dropper, children's medicine spoon, or oral syringe.



● When taking liquid medicines, make sure you shake the bottle thoroughly before measuring each dose, or you may take improper dosages if the active substance has risen to the top or settled at the bottom of the bottle.

● A drink of cold water immediately after an unpleasantly flavoured medicine may hide the taste and help prevent tablets from lodging in the oesophagus.

If you are taking several different drugs, ask your doctor if they can be taken together, or if they must be taken at different times in order to avoid any adverse effects or reduced effectiveness caused by an interaction between them.

How to take your drugs

If your prescription specifies taking your drug with food, or without, it is important to follow this instruction if you are to get the maximum benefit from your treatment.

Certain drugs, such as ampicillin, should be taken on an empty stomach (usually one to two hours before eating) in order for them to be absorbed more quickly into the bloodstream; others, such as ibuprofen, should be taken with food to avoid stomach irritation. Similarly, you should comply with any instructions to avoid particular foods. Milk and dairy products may inhibit the absorption of some drugs, such as tetracycline; grapefruit juice may affect the way certain drugs are broken down in the body and significantly increase their effectiveness; alcohol is best avoided with many drugs. (See also Drug interactions, p.16.)

Inhaled corticosteroids may sometimes cause fungal infections of the mouth and/or throat. These can be avoided to some degree by rinsing the mouth and gargling with water after each inhalation.

In some cases, when taking diuretics, for example, you may be advised to eat foods rich in potassium. But do not take potassium supplements or salt substitutes unless you are advised to do so by your doctor (see potassium, p.432).

GIVING MEDICINES TO CHILDREN

A number of over-the-counter medicines are specifically prepared for children. Many other medicines have labels that give both adult's and children's dosages. For the purposes of drug labelling, anyone 12 years of age or under is considered a child.

When giving over-the-counter medicines to children, you should always follow the instructions on the label exactly and under no circumstances exceed the dosage recommended for a child. Never give a child even a small amount of a medicine intended for adult use without the advice of your doctor.

Never leave a child's medicine within reach, and remember that adult's tablets may look like sweets. Also, be aware that apparently simple adult remedies may be extremely toxic to children at an adult dose (e.g. iron tablets).

MISSED DOSES

Missing a dose of your medication can be a problem only if you are taking the drug as part of a regular course of treatment. Missing a drug dose is not uncommon and it is not a cause for concern in most cases. The missed dose may sometimes produce a recurrence of symptoms or a change in the action of the drug, so you should know what to do when you have forgotten to take your medication. For advice on individual drugs, consult the drug profile in Part 3.

Additional measures

With some drugs, the timing of doses depends on how long the actions of the drugs last. When you miss a drug dose, the amount of drug in your body is lowered, and the drug's effect may be diminished. You may therefore have to take other steps to avoid unwanted consequences. For example, if you are taking a progesterone-only oral contraceptive and you forget to take one pill at your usual time, you may need to regard it as a missed pill (see What to do if you miss a pill, p.123); you should use another form of contraception.

If you miss more than one dose of any drug you are taking regularly, you should tell your doctor. Missed doses are especially important with insulin and drugs for epilepsy.

If you frequently forget to take your medication, you should tell your doctor. He or she may be able to simplify your treatment schedule by prescribing a multi-ingredient preparation that contains several drugs, or a preparation that releases the drug slowly into the body over a period of time, and only needs to be taken once or twice daily.

REMEMBERING YOUR MEDICATION

If you take several different drugs, it is useful to draw up a chart to remind yourself of when each drug should be taken. This will also help anyone who looks after you, or a doctor who is unfamiliar with your treatment.

The example given here is of a dosage chart for an elderly woman suffering from arthritis and a heart condition who has trouble sleeping. Her doctor has prescribed the following treatment:

Bumetanide (a diuretic to counter fluid retention), one 1mg tablet in the morning.

Amiloride (another diuretic to counter the potassium loss caused by bumetanide), two 5mg tablets in the morning.

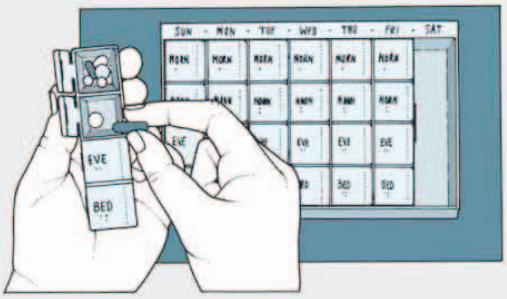
Ibuprofen (for arthritis), three 400mg tablets daily with meals.

Verapamil (to treat her heart condition), three 40mg tablets a day.

Zopiclone (a sleeping drug), one 3.75mg tablet at bedtime.

Dosage Chart

8am	1pm
1 x Bumetanide	1 x Ibuprofen
2 x Amiloride	1 x Verapamil
1 x Ibuprofen	
1 x Verapamil	
7pm	**11pm**
1 x Ibuprofen	1 x Verapamil
	1 x Zopiclone



Pill, or dosette, box
Using a pill box is a handy way of making sure you take your tablets in the right order. They are also very useful for carers of people with dementia. The boxes have a strip for each day of the week, and compartments for morning, afternoon, evening, and bedtime.

ENDING DRUG TREATMENT

As with missed doses, ending drug treatment too soon can be a problem when you are taking a regular course of drugs. With medication taken as required, you can stop as soon as you feel better.

Advice on stopping individual drugs is given in the drug profiles in Part 3. Some general guidelines for ending drug treatment are given below.

Risks of stopping too soon

Suddenly stopping drug treatment before completing your course of medication may cause the original condition to recur or lead to other complications, including withdrawal symptoms. The disappearance of the symptoms does not necessarily mean that a disorder is cured. Even if you feel better, do not stop taking the drug until the course has finished unless your doctor advises you to do so. People taking antibiotics often stop too soon, but the full course of treatment prescribed should always be followed.

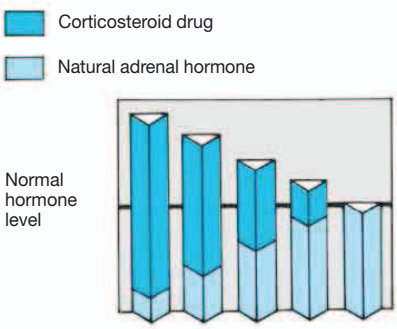
Adverse effects

Do not stop taking a medication simply because it produces unpleasant side effects. These often disappear or become bearable after a while. But if they do not, check with your doctor, who may want to reduce the dosage of the drug gradually or, alternatively, substitute another drug that does not produce the same side effects.

Gradual reduction

While many medications can be stopped abruptly, others need to be reduced gradually to prevent a reaction when treatment ends. This is the case with long-term corticosteroid therapy (see right) as well as with some antidepressants and dependence-inducing drugs.

Phased reduction of corticosteroids



Corticosteroid drugs suppress production in the body of natural adrenal hormones. A phased reduction of the dosage allows levels of the natural hormones to revert to normal. The last stages of withdrawal are made very slowly.

STORING DRUGS

Once you have completed a medically directed course of treatment, you should not keep any unused drugs. But most families will want to keep a supply of remedies for indigestion, headaches, colds, and so forth. Such medicines should not be used if they show any signs of deterioration, or if their period of effectiveness has expired (see When to dispose of drugs, right).

How to store drugs

All drugs, including cough medicines, iron tablets, and oral contraceptives, should be kept out of the reach of children. If you are in the habit of keeping your medicines where you will see them as a reminder to take them, leave an empty medicine container out instead, and put the drug itself safely out of reach.

Over-the-counter and prescription drugs should normally be stored in the container in which you purchased them. If it is necessary to put them into other containers, such as special containers designed for the elderly, make sure you keep the original container with the label, as well as any separate instructions, for future reference.

Make certain that caps and lids are replaced and tightly closed after use; loose caps may leak and spill, or hasten deterioration of the drug.

Where to store drugs

The majority of drugs should be stored in a cool, dry place out of direct sunlight, even those in plastic containers or tinted glass. Room temperature, away from sources of direct heat, is suitable for most medicines. A few drugs should be stored in the refrigerator. Storage information for individual drugs is given in the drug profiles in Part 3.

Wall cabinets that can be locked are ideal for storing drugs, as long as the cabinet itself is located in a cool, dry place and not, as often happens, in the bathroom, which is frequently warm and humid.

WHEN TO DISPOSE OF DRUGS

Old drugs should be flushed down the toilet or returned to the pharmacist, but not put in the dustbin. Always dispose of:

- Any drug that is past its expiry date.
- Aspirin and paracetamol tablets that smell of vinegar.
- Tablets that are chipped, cracked, or discoloured, and capsules that have softened, cracked, or stuck together.
- Liquids that have thickened or discoloured, or that taste or smell different in any way from the original product.
- Tubes that are cracked, leaky, or hard.
- Ointments and creams that have changed odour, or changed appearance by discolouring, hardening, or separating.
- Any liquid needing refrigeration that has been kept past its expiry date.

LONG-TERM DRUG TREATMENT

Many people require regular, prolonged treatment with one or more drugs. People who suffer from chronic or recurrent disorders often need lifelong treatment with drugs to control symptoms or prevent complications. Antihypertensive drugs for high blood pressure and insulin or oral antidiabetic drugs for diabetes mellitus are familiar examples. Many other disorders take a long time to cure; for example, people with tuberculosis usually need at least six months' treatment with antituberculous drugs. Long-term drug treatment may also be necessary to prevent a condition from occurring, and will have to be taken for as long as the individual is at risk. Antimalarial drugs are a good example.

Possible adverse effects

You may worry that taking a drug for a long period will reduce its effectiveness or that you will become dependent on it. However, tolerance develops only with a few drugs; most medicines continue to have the same effect indefinitely without necessitating an increase in dosage or change in drug. Similarly, taking a drug for more than a few weeks does not normally create dependence.

Changing drug treatment

If you are taking a drug regularly, you will need to know what to do if something else occurs to affect your health. If you wish to become pregnant, for example, you should ask your doctor right away if it is preferable to continue on your regular medicine or switch to another less likely to affect your pregnancy. If you contract a new illness, for which an additional drug is prescribed, your regular treatment may be altered.

There are a number of other reasons for changing a drug. You may have had an adverse reaction, or an improved preparation may have become available.

Adjusting to long-term treatment

You should establish a daily routine for taking your medication in order to reduce the risk of a missed dose. Usually you should not stop taking your medication, even if there are side effects, without consulting your doctor (see Ending drug treatment, facing page). If you fear possible side effects from the drug, discuss this with your doctor.

Many people deliberately stop their drugs because they feel well or their symptoms disappear. This can be dangerous, especially with a disease like high blood pressure, which has no noticeable symptoms. Stopping treatment may lead to a recurrence or worsening of a disease. If you are uncertain about why you have to keep taking a drug, ask your doctor.

Only a few drugs require an alteration in habits. Some drugs should not be taken with alcohol; with a few drugs you should avoid certain foods. If you require a drug that makes you drowsy, you should not drive a car or operate dangerous equipment.

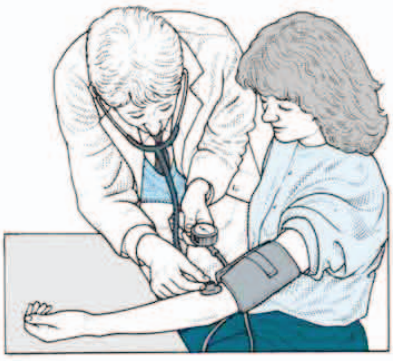
If you are allergic to a drug, or are taking one that should not be stopped suddenly or that may interact with other drugs, it is a good idea to carry a warning card or bracelet (MedicAlert for example). Such information might be essential for those giving emergency medical treatment in an accident.

Monitoring treatment

If you are on long-term treatment, you need to visit your doctor for periodic check-ups. He or she will check your underlying condition and monitor any adverse effects of treatment. Levels of the drug in the blood may be measured. With insulin, in addition to checks with the doctor, you need to monitor blood or urine levels each day.

If a drug is known to cause damage to an organ, tests may be done to check the function of the organ. For example, blood and urine tests to check kidney function, or a blood count to check the bone marrow, may be indicated.

Medical check-ups
Blood pressure is commonly checked in people on long-term drug treatment.



EXCEEDING THE DOSE

Most people associate drug overdoses with attempts at suicide or the fatalities and near fatalities brought on by abuse of street drugs. However, drug overdoses can also occur among people who deliberately or inadvertently exceed the stated dose of a drug that has been prescribed for them by their doctor.

A single extra dose of most drugs is unlikely to be a cause for concern, although accidental overdoses can create anxiety in the individual and his or her family, and may cause overdose symptoms, which can appear in a variety of different forms.

Overdose of some drugs, however, is potentially dangerous even when the dose has been exceeded by only a small amount. Each of the drug profiles in Part 3 gives detailed information on the consequences of exceeding the dose, symptoms to look out for, and what to do. Each drug has an overdose danger rating of low, medium, or high, which are described fully on p.146.

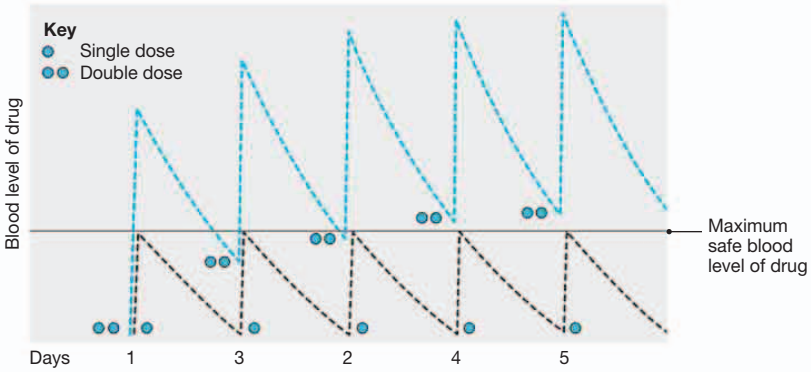
Taking an extra dose

People sometimes exceed the stated dose in the mistaken belief that by increasing dosage they will obtain more immediate action or a more effective cure. This action is a particular risk with tolerance-inducing drugs (see Drug tolerance and dependence, p.23). Others exceed their dose accidentally, by miscalculating the amount or forgetting that the dose has already been taken.

Taking extra doses is often a problem in the elderly, who may repeat their dose through forgetfulness or confusion. This is a special risk with medicines that cause drowsiness (see also p.22).

In some cases, especially when liver or kidney function deteriorates, the drug builds up in the blood because the body cannot break down and excrete the extra dose quickly enough, so that symptoms of poisoning may result. Symptoms of excessive intake may not be apparent for many days.

Effects of repeated overdose
Too high a dose of a drug over an extended period may lead to a build-up of high levels of the drug in the body, especially if liver or kidney function is reduced.



When and how to get help

If you are not sure whether or not you have taken your medicine, think back and check again. If you honestly cannot remember, assume that you have missed the dose and follow the advice given in the individual drug profiles in Part 3 of this book. If you cannot find your drug, consult your doctor. Make a note to use some system in the future which will help you remember to take your medicine.

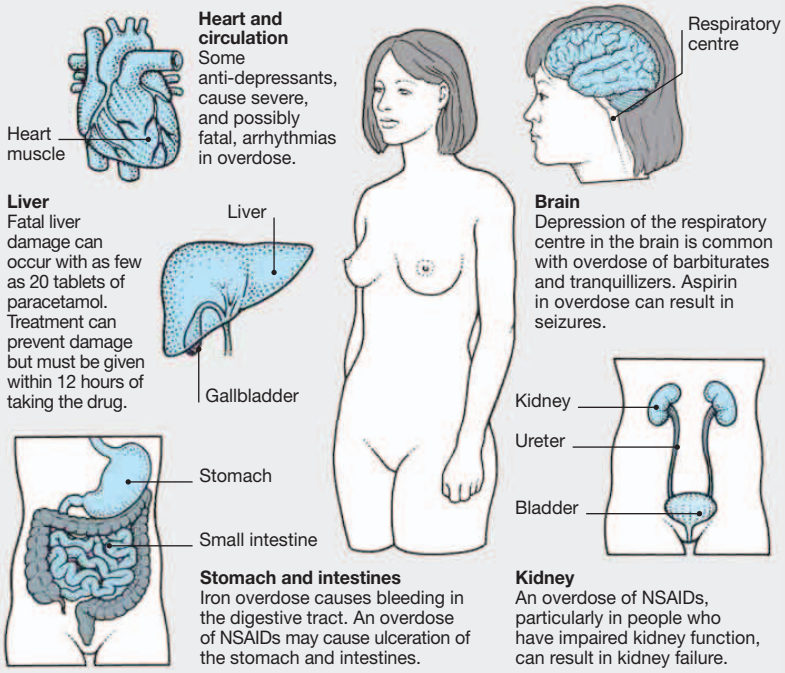
If you are looking after an elderly person on regular drug treatment who suddenly develops unusual symptoms such as confusion, drowsiness, or unsteadiness, consider the possibility of an inadvertent drug overdose and consult the doctor as soon as possible.

Deliberate overdose

While many cases of drug overdose are accidental or the result of a mistaken belief that increasing the dose will enhance the benefits of drug treatment, sometimes an excessive amount of a drug is taken with the intention of causing harm or even as a suicide attempt. Whether or not you think a dangerous amount of a drug has been taken, deliberate overdoses of this kind should always be brought to the attention of your doctor. Not only is it necessary to ensure that no physical harm has occurred as a result of the overdose, but the psychological condition of a person who takes such action may indicate the need for additional medical help, especially when the person is elderly, has a physical illness, or is known to suffer from depression.

THE EFFECT OF DRUG OVERDOSE ON THE BODY

The effect of drug overdose on the body depends on the type of drug involved. Some drugs produce an exaggeration of the desired effect, for instance overdose of tranquillizers leads to unconsciousness. With many drugs, the toxic overdose effects are unrelated to the action or side effects of the drug when it is taken in normal doses.


Heart muscle
Heart and circulation
Some anti-depressants, cause severe, and possibly fatal, arrhythmias in overdose.
Respiratory centre
Liver
Liver
Fatal liver damage can occur with as few as 20 tablets of paracetamol. Treatment can prevent damage but must be given within 12 hours of taking the drug.
Brain
Depression of the respiratory centre in the brain is common with overdose of barbiturates and tranquillizers. Aspirin in overdose can result in seizures.
Gallbladder
Kidney
Ureter
Bladder
Stomach
Small intestine
Stomach and intestines
Iron overdose causes bleeding in the digestive tract. An overdose of NSAIDs may cause ulceration of the stomach and intestines.
Kidney
An overdose of NSAIDs, particularly in people who have impaired kidney function, can result in kidney failure.

DOs AND DON'Ts

On this page you will find a summary of the most important practical points concerning the management of your drug treatment. The advice is arranged under general headings, explaining the safest methods of storing drugs and following treatment, whether it is a prescribed medicine or an over-the-counter drug. This information is equally applicable whether you are taking medicine yourself or supervising the drug treatment of someone in your care.

At the surgery or in hospital

DO

✓ Tell the person prescribing your drugs about all drugs you are already taking, including prescription or over-the-counter drugs, complementary or alternative medicine, and street drugs.
✓ Tell them if you are pregnant, intending to become pregnant, or breast-feeding.
✓ Tell them about any allergic reactions you have experienced to past drug treatments.
✓ Tell them if you have a current health problem, such as liver disease, or if you think you might be at risk from drug treatment for any other reason.
✓ Discuss your drug treatment with the person prescribing your drugs and make sure you understand why you have been given a particular drug and what benefits you can expect. Often, people who do not understand the reasons for their treatment fail to take their drug correctly. Take your medicines with you when you go into hospital to ensure that the doctors know what you are taking.

DON'T

✗ Leave the surgery or hospital before you understand clearly how and when to take the drug.

At the pharmacy

DO

✓ Ask your pharmacist's advice about over-the-counter drugs if you are not sure what you should buy, or if you think you may react adversely to a drug.
✓ Try to see the same pharmacist or use the same pharmacy to obtain your regular prescriptions.
✓ Be sure you know the name of the drug you have been prescribed. If you are getting a repeat prescription and your doctor has specified that you should always use the same brand, make sure the brand is correct.
✓ Make sure you understand what is on the drug label.
✓ Ask the pharmacist to put your drug in a container with an easy-to-remove cap if you have difficulty using child-resistant containers

DON'T

✗ Send children to the pharmacy to get your medicine for you.

Giving medicines to children

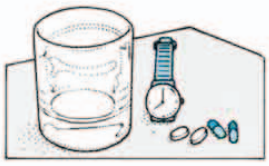
DO

✓ Check the dose on the label carefully before giving medicines to children.
✓ Make sure over-the-counter preparations you give to children under 16 years old do not contain aspirin.
✓ Make sure you use the special measuring spoon or oral syringe to administer doses from a liquid preparation more accurately and easily.

DON'T

✗ Pretend to children that medicines are sweets or soft drinks.
✗ Give any medicines to children under the age of five, except on the advice of your doctor.

Taking your drug



DO

✓ Make sure that your drug will not make you drowsy or otherwise affect your ability before you drive or perform difficult or dangerous tasks.
✓ Read the label carefully and do what it says. This is equally important with all types of drugs, creams, and lotions as well as drugs taken by mouth.
✓ Finish the drug treatment prescribed for you.
✓ Consult your doctor for advice if you experience side effects.

DON'T

✗ Take any prescribed or over-the-counter drugs without first consulting your doctor if you are pregnant or trying to conceive.
✗ Take any drugs after the expiry date has passed.
✗ Miss any doses; if you have trouble remembering to take your medicine, talk your doctor or pharmacist.
✗ Offer your medicine to other people or take medicine that has been prescribed for someone else (even if the symptoms are the same).

Food, drink, and drugs of abuse

DO

✓ Check whether it is safe to take alcohol with the drugs you have been prescribed.
✓ Check that there are no foods you should avoid.
✓ Follow the timing of your drugs with respect to meals, when instructed to do so by your doctor or pharmacist.

DON'T

✗ Take drugs (except those prescribed by your doctor or other qualified prescriber) or alcohol if you are pregnant or trying to conceive. They may adversely affect the unborn baby.
✗ Take drugs of abuse under any circumstances.

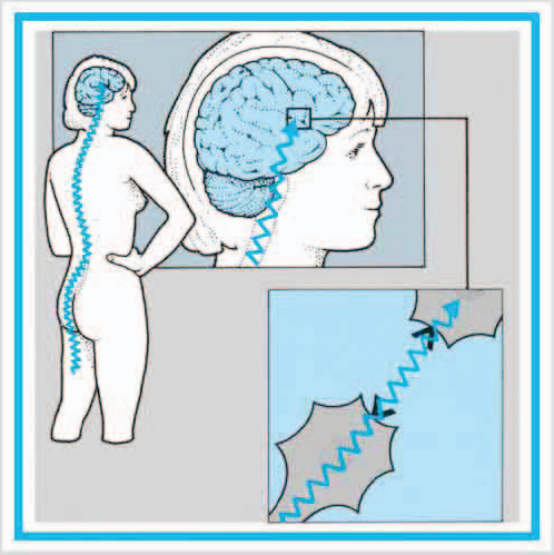
Storing drugs

DO

✓ Take care to store drugs in a cool, dry place and protect them from light or refrigerate them, if advised to do so.
✓ Keep all drugs, including seemingly harmless ones such as cough preparations, locked away out of the reach of children.
✓ Check your medicine chest regularly in case other members of the family have left their unwanted drugs in it, and to make sure that none of the normal supplies are out of date.
✓ Keep drugs in their original containers with the original instructions to avoid confusion.

DON'T

✗ Hoard drugs at home. When you have stopped taking a prescribed drug, dispose of it unless it is part of your family first aid kit.



PART

2

MAJOR DRUG GROUPS

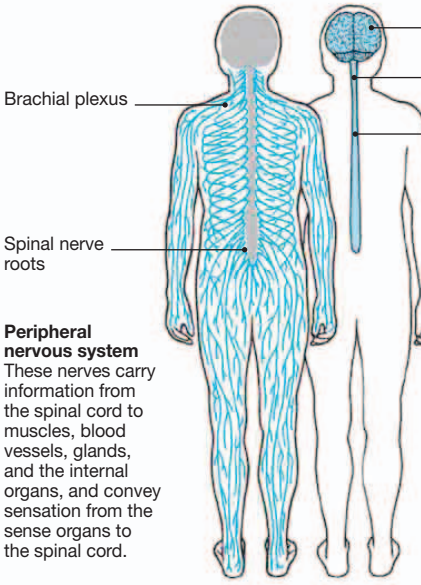
BRAIN AND NERVOUS SYSTEM
RESPIRATORY SYSTEM
HEART AND CIRCULATION
GASTROINTESTINAL TRACT
MUSCLES, BONES, AND JOINTS
ALLERGY
INFECTIONS AND INFESTATIONS
HORMONES AND ENDOCRINE SYSTEM
NUTRITION
MALIGNANT AND IMMUNE DISEASE
REPRODUCTIVE AND URINARY TRACTS
EYES AND EARS
SKIN

BRAIN AND NERVOUS SYSTEM

The human brain contains more than 100 billion nerve cells (neurons). These nerve cells receive electrochemical impulses from everywhere in the body. They interpret these impulses and send responsive signals back to various glands and muscles. The brain functions continuously as a switchboard for the human communications system. At the same time, it serves as the seat of emotions and mood, of memory, personality, and thought. Extending from the brain is an additional, large rod-shaped cluster of nerve cells that forms the spinal cord. Together, these two elements comprise the central nervous system.

Radiating from the central nervous system is the peripheral nervous system, which has three parts. One branches off the spinal cord and extends to skin and muscles throughout the body. Another, in the head, links the brain to the eyes, ears, nose, and taste buds. The third is a semi-independent network called the autonomic, or involuntary, nervous system. This is the part of the nervous system that controls unconscious body functions such as breathing, digestion, and glandular activity (see facing page).

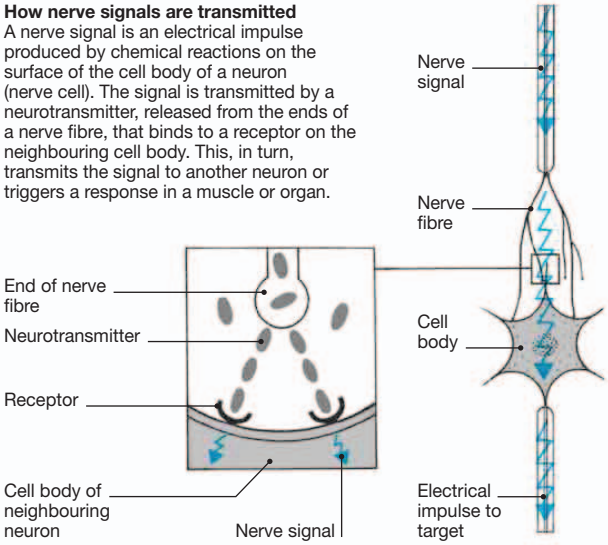
Signals traverse the nervous system by electrical and chemical means. Electrical impulses carry signals from one end of a neuron to the other. To cross the gap between neurons, chemical neurotransmitters are released from one cell to bind on to the receptor sites of nearby cells. Excitatory transmitters stimulate action; inhibitory transmitters reduce it.



Peripheral nervous system
These nerves carry information from the spinal cord to muscles, blood vessels, glands, and the internal organs, and convey sensation from the sense organs to the spinal cord.

Central nervous system
The central nervous system contains billions of interconnecting nerve cells that receive and transmit signals to, and from the peripheral nerves.

How nerve signals are transmitted
A nerve signal is an electrical impulse produced by chemical reactions on the surface of the cell body of a neuron (nerve cell). The signal is transmitted by a neurotransmitter, released from the ends of a nerve fibre, that binds to a receptor on the neighbouring cell body. This, in turn, transmits the signal to another neuron or triggers a response in a muscle or organ.



What can go wrong

Disorders of the brain and nervous system may manifest as illnesses that show themselves as physical impairments, such as epilepsy or strokes, or as mental and emotional impairments (for example, schizophrenia or depression).

Illnesses causing physical impairments can result from different types of disorder of the brain and nervous system. Death of nerve cells resulting from poor circulation can result in paralysis, while electrical disturbances of certain nerve cells cause the seizures of epilepsy. Temporary changes in blood circulation within and around the brain are associated with migraine. Parkinson's disease is caused by a lack of dopamine, a neurotransmitter that is produced by specialized brain cells.

The causes of disorders that trigger mental and emotional impairment are not known, but these illnesses are thought to result from the defective functioning of nerve cells and neurotransmitters. The nerve cells may be underactive, overactive, or poorly coordinated. Alternatively, mental and emotional impairment may be due to too much or too little neurotransmitter in one area of the brain.

Why drugs are used

By and large, the drugs described in this section do not eliminate nervous system disorders. Their function is to correct or modify the communication of the signals that traverse the nervous system. By doing so they can relieve symptoms or restore normal functioning and behaviour. In some cases,

AUTONOMIC NERVOUS SYSTEM

The autonomic, or involuntary, nervous system governs the actions of the muscles of the organs and glands. Such vital functions as heart beat, salivation, and digestion continue without conscious direction, whether we are awake or asleep.

The autonomic system is divided into two parts, the effects of one generally balancing those of the other. The sympathetic nervous system has an excitatory effect. For example, it widens the airways to the lungs, increases the heart rate, and increases the flow of blood to the arms and legs. The parasympathetic system, by contrast, has an opposing effect. It slows the heart rate, narrows the large airways, and redirects blood from the limbs to the gut.

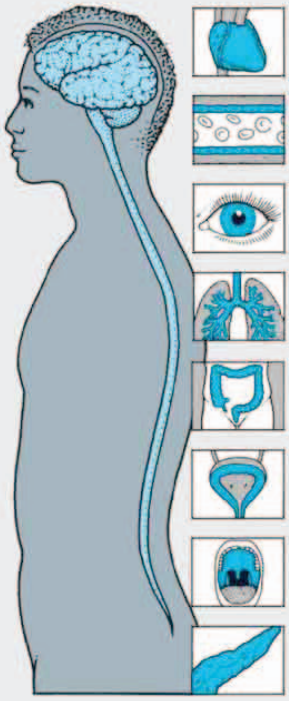
Although the functional pace of most organs results from the interplay between the two systems, the muscles surrounding the blood vessels respond only to the signals of the sympathetic system. Whether a vessel is dilated or constricted is determined by the relative stimulation of two sets of receptor sites: alpha sites and beta sites.

Neurotransmitters
The parasympathetic nervous system depends on the neurotransmitter acetylcholine to transmit signals from one cell to another. The sympathetic nervous system relies on adrenaline and noradrenaline, substances that act as both hormones and neurotransmitters.

Drugs that act on the sympathetic nervous system
The drugs that stimulate the sympathetic nervous system are called adrenergics (or sympathomimetics, see chart). They either promote the release of adrenaline and noradrenaline or mimic their effects. Drugs that interfere with the action of the sympathetic nervous system are called sympatholytics. Alpha blockers act on alpha receptors; beta blockers act on beta receptors (see also Beta blockers, p.55).

Drugs that act on the parasympathetic nervous system
Drugs that stimulate the parasympathetic nervous system are called cholinergics (or parasympathomimetics), and drugs that oppose its action are called anticholinergics. Many prescribed drugs have anticholinergic properties (see chart, right).

Effects of stimulation of the autonomic nervous system



	Sympathetic	Parasympathetic
Heart	The rate and strength of the heart beat are increased.	The rate and strength of the heart beat are reduced.
Blood vessels in skin	These are constricted by stimulation of alpha receptors.	No effect.
Pupils	The pupils are dilated.	The pupils are constricted.
Airways	The bronchial muscles relax and widen the airways.	The bronchial muscles contract and narrow the airways.
Intestines	Activity of the muscles of the intestinal wall is reduced.	Activity of the muscles of the intestinal wall is increased.
Bladder	The bladder wall relaxes and the sphincter muscle contracts.	The bladder wall contracts and the sphincter muscle relaxes.
Salivary glands	Secretion of thick saliva increases.	Secretion of watery saliva increases.
Pancreas	Insulin secretion is increased (beta receptors) or reduced (alpha receptors).	Insulin secretion is increased.

Drugs that act on the autonomic nervous system

	Sympathetic	Parasympathetic
Stimulated by		
Natural neurotransmitters	Epinephrine (adrenaline) Norepinephrine (noradrenaline)	Acetylcholine
Drugs	Adrenergic drugs (including alpha agonists, beta agonists) Sympathomimetics	Cholinergic drugs Parasympathomimetics
Blocked by		
Drugs	Alpha blockers (antagonists) Beta blockers (antagonists)	Anticholinergic drugs

such as anxiety and insomnia, drugs are used to lower the level of activity in the brain. In other disorders – depression, for example – drugs are given to encourage the opposite effect, increasing the level of activity.

Drugs that act on the nervous system are also used for conditions that outwardly have nothing to do with nervous system disorders. Vomiting, for example, may be treated with drugs that directly affect the vomiting centre in the brain or block stimulatory nerve signals to the vomiting centre.

MAJOR DRUG GROUPS

Analgesics
Sleeping drugs
Anti-anxiety drugs
Antidepressant drugs
Antipsychotic drugs
Anticonvulsant drugs
Drugs for parkinsonism
Drugs for dementia
Nervous system stimulants
Drugs for migraine
Anti-emetics

ANALGESICS

Analgesics (painkillers) are drugs that relieve pain. Since pain is not a disease but a symptom, long-term relief depends on treatment of the underlying cause. For example, the pain of toothache can be relieved by drugs but can be cured only by appropriate dental treatment. If the underlying disorder is irreversible, such as some rheumatic conditions, long-term analgesic treatment may be necessary.

Damage to body tissues as a result of disease or injury is detected by nerve endings that transmit signals to the brain. The interpretation of these sensations can be affected by the psychological state of the individual, so that pain is worsened by anxiety and fear, for example. Often a reassuring explanation of the cause of discomfort can make pain easier to bear and may even relieve it altogether. Anti-anxiety drugs (see p.39) are helpful when pain is accompanied by anxiety, and some of these drugs are also used to reduce painful muscle spasms. Some antidepressant drugs (see p.40) act to block the transmission of impulses signalling pain and are particularly useful for nerve pains (neuralgia), which do not always respond to analgesics.

Types of analgesics

Analgesics are divided into the opioids (with similar properties to drugs derived from opium, such as morphine) and non-opioids. Non-opioids include all the other analgesics, including paracetamol, nefopam, and also the non-steroidal anti-inflammatory drugs (NSAIDs), the most well known of which is aspirin. The non-opioids are all less powerful as painkillers than the opioids. Local anaesthetics are also used to relieve pain (see below).

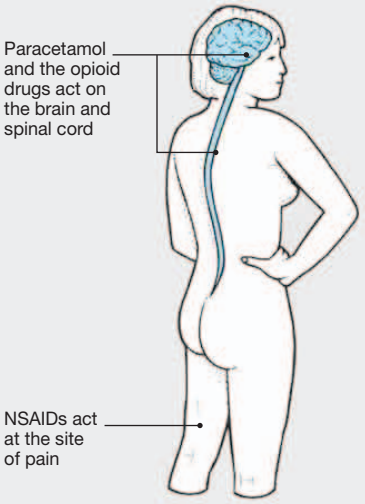
Opioid drugs and paracetamol act directly on the brain and spinal cord to alter the perception of pain. Opioids act like the endorphins, hormones naturally produced in the brain that stop the cell-to-cell transmission of pain sensation. NSAIDs block the formation of pain-modulating substances (e.g. prostaglandins) at nerve endings at the site of pain.

When pain is treated under medical supervision, it is common to start with paracetamol or an NSAID; if neither provides adequate pain relief, they may be combined. A mild opioid (for example, codeine) may also be used. If the less powerful drugs are ineffective, a strong opioid such as morphine may be given. As there is now a wide variety of oral analgesic formulations, injections are seldom necessary to control even the most severe pain.

When treating pain with an over-the-counter preparation, for example, taking paracetamol for a headache, you should seek medical advice if pain persists for longer than 48 hours, recurs, or is worse or different from previous pain.

SITES OF ACTION

Paracetamol and the opioid drugs act on the brain and spinal cord to reduce pain perception. Non-steroidal anti-inflammatory drugs (NSAIDs) act at the site of pain to prevent the stimulation of nerve endings.



Non-opioid analgesics

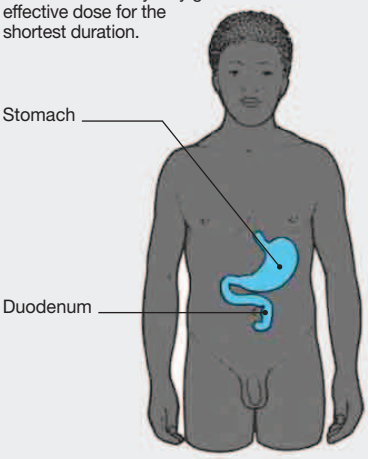
Paracetamol

This analgesic is believed to act by reducing the production of chemicals called prostaglandins in the brain. However, paracetamol does not affect prostaglandin production in the rest of the body, so it does not reduce inflammation, although it can reduce fever. Paracetamol can be used for everyday aches and pains, such as headaches, toothache, and joint pains.

As well as being the most widely used analgesic, it is one of the safest when taken correctly. It does not usually irritate the stomach and allergic reactions are rare. However, an overdose can cause severe and possibly fatal liver or kidney damage. Its toxic potential may be increased in heavy drinkers.

NSAIDs AND DIGESTIVE TRACT IRRITATION

NSAIDs can cause irritation, even ulceration and bleeding, of the stomach and duodenum, so they are best taken after a meal. NSAIDs are not usually given to people with stomach ulcers. An NSAID may be combined with an anti-ulcer drug (see p.67). In certain cases, a COX-2 inhibitor may be used. However, NSAIDs are usually only given in the lowest effective dose for the shortest duration.



Non-steroidal anti-inflammatory drugs (NSAIDs): aspirin

Used for many years to relieve pain and reduce fever, aspirin also acts to reduce inflammation by blocking the production of prostaglandins, which contribute to the swelling and pain in inflamed tissue (see Action of analgesics, facing page). Aspirin is useful for headaches, toothache, mild rheumatic pain, sore throat, and discomfort caused by feverish illnesses. Given regularly, it can also relieve the

LOCAL ANAESTHETICS

These drugs are used to prevent pain, usually in minor surgical procedures, for example, dental treatment and stitching cuts. They can also be injected into the space around the spinal cord to numb the lower half of the body. This is called spinal or epidural anaesthesia and can be used for some major operations in people who are not fit for a general anaesthetic. Epidural anaesthesia is also used during childbirth.

Local anaesthetics block the passage of nerve impulses at the site of administration, deadening all feeling conveyed by the nerves they come into contact with. They do not, however, interfere with consciousness. Local anaesthetics are usually given by injection, but they can also be applied to the skin, the mouth and other areas lined with mucous membrane (such as the vagina), or the eye to relieve pain. Some local anaesthetics are formulated for injection together with epinephrine (adrenaline). Epinephrine constricts the blood vessels and prevents the local anaesthetic from being removed. This action prolongs the anaesthetic's effect.

Local anaesthetic creams are often used to numb the skin before injections in children and people with a fear of needles.

pain and inflammation of chronic rheumatoid arthritis (see Antirheumatic drugs, p.75).

Aspirin is found in combination with other substances in a variety of medicines (see Cold cures, p.52). It is also used in the treatment of some blood disorders, since aspirin helps to prevent abnormal clotting of blood by preventing platelets from sticking together (see Drugs that affect blood clotting, p.62).

Aspirin in the form of soluble tablets, dissolved in water before being taken, is absorbed into the bloodstream more quickly, thereby relieving pain faster than tablets. Soluble aspirin is not, however, less irritating to the stomach lining.

Aspirin is available in many forms, all of which have a similar effect, but because the amount of aspirin in a tablet of each type varies, it is important to read the packet for the correct dosage. It is not recommended for children aged under 16 years because its use has been linked to Reye's syndrome, a rare but potentially fatal liver and brain disorder.

Other non-steroidal anti-inflammatory drugs (NSAIDs)

These drugs can relieve both pain and inflammation. NSAIDs are related to aspirin and also work by blocking the production of prostaglandins. They are most commonly used to treat muscle and joint pain and may also be prescribed for other types of pain including period pain. For further information on these drugs, see p.74.

Combined analgesics

Mild opioids, such as codeine, are often found in combination preparations with non-opioids, such as paracetamol. The prefix "co-" is used to denote a drug combination. Although both opioids and paracetamol act centrally, these mixtures have the advantage of combining different mechanisms of action. Another advantage of combining analgesics is that the reductions in dose of the components may reduce the side effects of the preparation. Combinations can be helpful in reducing the number of tablets taken during long-term treatment.

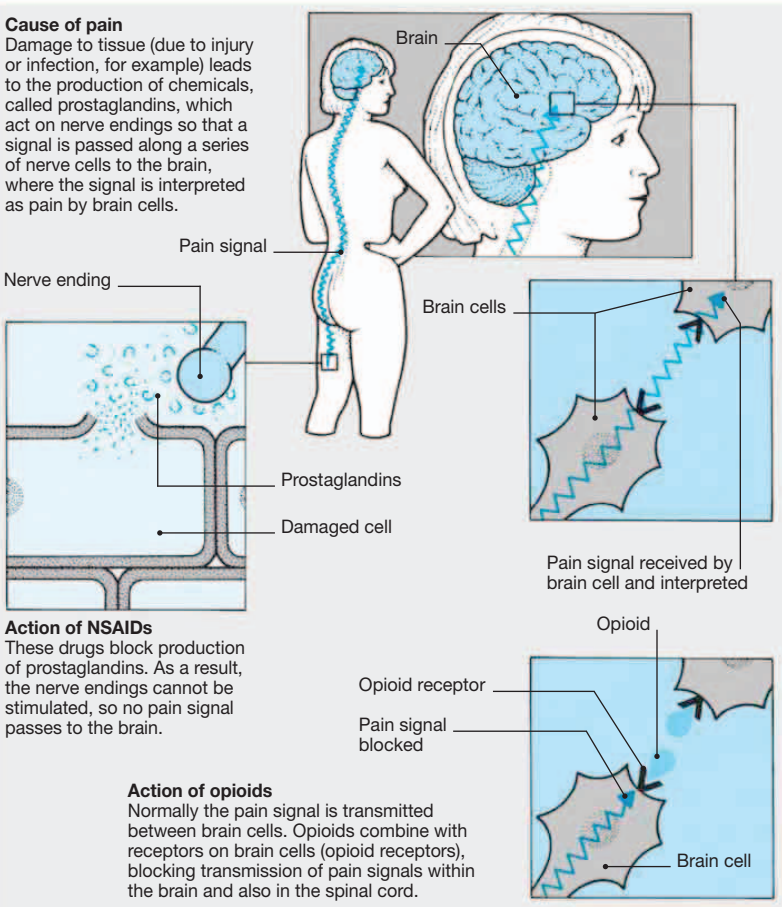
Opioid analgesics

These drugs are related to opium, an extract of poppy seeds. They act directly on several sites in the central nervous system to block the transmission of pain signals (see Action of analgesics, above). Because they act directly on the parts of the brain where pain is perceived, opioids are the strongest analgesics and are therefore used to treat the pain arising from surgery, serious injury, and cancer. These drugs are particularly valuable for relieving severe pain during terminal illnesses. In addition, their ability to produce a state of relaxation and euphoria is often of help in relieving the stress that accompanies severe pain. Morphine is the best known opioid analgesic. Others include diamorphine (heroin) and pethidine. The use of these powerful opioids is strictly controlled because the euphoria produced can lead to abuse and addiction. When these opioids are given under medical supervision to treat severe pain, the risk of addiction is negligible.

Opioid analgesics may prevent clear thought and cloud consciousness. Other possible adverse effects include nausea, vomiting, constipation, drowsiness, and depressed breathing. When they are taken in overdose, these drugs may induce a deep coma and lead to fatal breathing difficulties.

In addition to the powerful opioids, there are some less powerful drugs in this group that are used to relieve mild to moderate pain. They include codeine and tramadol. The opioids' normally unwanted side effects of depressing respiration and causing constipation make them useful as cough suppressants (p.52) and as antidiarrhoeal drugs (p.68).

ACTION OF ANALGESICS


Cause of pain
Damage to tissue (due to injury or infection, for example) leads to the production of chemicals, called prostaglandins, which act on nerve endings so that a signal is passed along a series of nerve cells to the brain, where the signal is interpreted as pain by brain cells.
Brain
Pain signal
Nerve ending
Brain cells
Prostaglandins
Damaged cell
Pain signal received by brain cell and interpreted
Action of NSAIDs
These drugs block production of prostaglandins. As a result, the nerve endings cannot be stimulated, so no pain signal passes to the brain.
Opioid
Opioid receptor
Pain signal blocked
Brain cell
Action of opioids
Normally the pain signal is transmitted between brain cells. Opioids combine with receptors on brain cells (opioid receptors), blocking transmission of pain signals within the brain and also in the spinal cord.

COMMON DRUGS

Opioids
Buprenorpine
Co-codamol
Codeine ✻
Co-dydramol
Diamorphine (heroin)
Dihydrocodeine ✻
Dipipanone
Fentanyl
Meptazinol
Methadone ✻
Morphine ✻
Oxycodone
Pethidine
Tramadol ✻

✻ See Part 3

NSAIDs (see p.74)
Aspirin ✻
Diclofenac ✻
Etodolac
Fenbufen
Fenoprofen
Ibuprofen ✻
Indometacin
Ketoprofen ✻
Meloxicam ✻
Mefenamic acid ✻
Naproxen ✻
Piroxicam ✻

Other non-opioids
Nefopam
Paracetamol ✻

SLEEPING DRUGS

Difficulty in getting to sleep or staying asleep (insomnia) has many causes. Most people suffer from sleepless nights from time to time, usually as a result of a temporary worry or discomfort from a minor illness. Persistent sleeplessness can be caused by psychological problems including anxiety or depression, or by pain and discomfort arising from a physical disorder.

Why they are used

For occasional bouts of sleeplessness, simple, common remedies to promote relaxation – for example, taking a warm bath or a hot milk drink before bedtime – are usually the best form of treatment. Sleeping drugs (also known as hypnotics) are normally prescribed only when these self-help remedies have failed, and when lack of sleep is beginning to affect your general health. These drugs are used to re-establish the habit of sleeping. They should be used in the smallest dose and for the shortest possible time (not more than three weeks). It is best not to use sleeping tablets every night (see Risks and special precautions, right). Do not use alcohol to get to sleep as it can cause disturbed sleep and insomnia. Long-term treatment of sleeplessness depends on resolving the underlying cause of the problem.

How they work

Most sleeping drugs promote sleep by depressing brain function. The drugs interfere with chemical activity in the brain and nervous system by reducing communication between nerve cells. This leads to reduced brain activity, allowing you to fall asleep more easily, but the nature of the sleep is affected by the drug. The main class of sleeping drugs, the benzodiazepines, is described on the facing page.

How they affect you

A sleeping drug rapidly produces drowsiness and slowed reactions. Some people find that the drug makes them appear to be drunk, their speech slurred, especially if they delay going to bed after taking their dose. Most people find they usually fall asleep within one hour of taking the drug.

Because the sleep induced by drugs is not the same as normal sleep, many people find they do not feel as well rested by it as by a night of natural sleep. This is the result of suppressed brain activity. Sleeping drugs also suppress the sleep during which dreams occur; both dream sleep and non-dream sleep are essential for a good night's sleep (see The effects of drugs on sleep patterns, below).

Some people experience a variety of hangover effects the following day. Some benzodiazepines may produce minor side effects, such as daytime drowsiness, dizziness, and unsteadiness, that can impair the ability to drive or operate machinery. Elderly people are likely to become confused and selection of an appropriate drug is important.

Risks and special precautions

Sleeping drugs become less effective after the first few nights and there may be a temptation to increase the dose. Apart from the antihistamines, most sleeping drugs can produce psychological and physical dependence (see p.23) when taken regularly for more than a few weeks, especially if they are taken in larger-than-normal doses.

When sleeping drugs are suddenly withdrawn, anxiety, seizures, and hallucinations sometimes occur. Nightmares and vivid dreams may be a problem because the time spent in dream sleep increases. Sleeplessness will recur and may lead to a temptation to use sleeping drugs again. Anyone who wishes to stop taking sleeping drugs, particularly after prolonged use, should seek his or her doctor's advice to prevent these withdrawal symptoms from occurring.

TYPES OF SLEEPING DRUGS

Benzodiazepines These are the most commonly used class of sleeping drugs as they have comparatively few adverse effects and are relatively safe in overdose. They are also used to treat anxiety (see facing page).

Barbiturates These are now almost never used because of the risks of abuse, dependence, and toxicity in overdose. There is also a risk of prolonged sedation ("hangover").

Chloral derivatives These drugs effectively promote sleep but are little used now. If prescribed, triclofos causes fewer gastro-intestinal side effects than chloral hydrate.

Other non-benzodiazepine sleeping drugs Zopiclone, zaleplon, and zolpidem work in a similar way to benzodiazepines. They are not intended for long-term use and withdrawal symptoms have been reported.

Antihistamines Widely used to treat allergic symptoms (see p.82), antihistamines also cause drowsiness. They are sometimes used to promote sleep.

Antidepressant drugs Some of these drugs may be used to promote sleep in depressed people (see p.40), as well as being effective in treating underlying depressive illness.

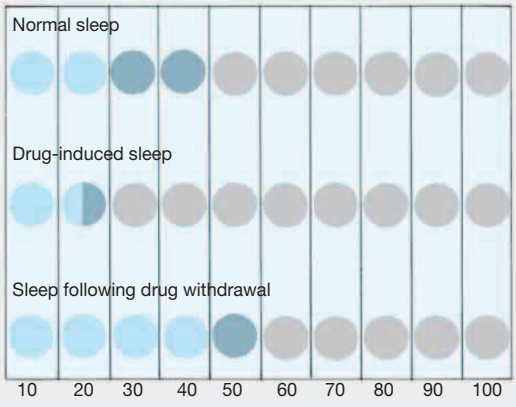
THE EFFECTS OF DRUGS ON SLEEP PATTERNS

Normal sleep can be divided into three types: light sleep, deep sleep, and dream sleep. The proportion of time spent in each type of sleep changes with age and is altered by sleeping drugs. Dramatic changes in sleep patterns also occur in the first few days following abrupt withdrawal of sleeping drugs after regular, prolonged use.

Normal sleep Young adults spend most sleep time in light sleep with roughly equal proportions of dream and deep sleep.

Drug-induced sleep has less dream sleep and less deep sleep with relatively more light sleep.

Sleep following drug withdrawal There is a marked increase in dream sleep, causing nightmares, following withdrawal of drugs used regularly for a long time.



COMMON DRUGS

Benzodiazepines
Flurazepam
Loprazolam
Lormetazepam
Nitrazepam ✻
Temazepam ✻

Other non-benzodiazepine sleeping drugs
Clomethiazole
Promethazine ✻
Zaleplon
Zolpidem
Zopiclone ✻

✻ See Part 3

Exploring the Variety of Random Documents with Different Content

“And—and there’s a certain amount of suffering,” added Mr. Dobb, watching his friend narrowly.

“Once I get me fingers on the twenty quid, I shall soon stop suffering,” asserted Mr. Tridge, cheerfully.

“Well, you remember me asking you just now if you’d ever ’ad a quarrel with a prize-fighter?”

“Yes, I remember. But what’s that to— ’Ere, ’strewth! ’Orace!” cried Mr. Tridge, in alarm. “I twig your game now! You’re wanting me to match against a prize-fighter! No, thanks!” he said, with the utmost firmness. “Once bit, twice shy!”

“Wait a bit!” begged Mr. Dobb. “You ’aven’t ’eard what I’ve got to say!”

“And don’t want to, either! Not if there’s a prize fight at the end of it! Not for fifty blessed quid! I’ve ’ad some! No, thank you, ’Orace. I ain’t fighting no prize-fighters on the thin chance of getting a purse of twenty quid—*if* I win. Not me, ’Orace!”

“But you won’t ’ark to what I say!” complained Mr. Dobb.

“No, I won’t!” asseverated Mr. Tridge. “While I’ve got the senses I was born with, I’ll ’ave nothing to do with prize-fighters, and that’s flat!”

“You mean it?” asked Horace. “That’s your last word?”

“I do!” returned Mr. Tridge, in complete determination. “It are!”

Mr. Dobb shook his head a little perplexedly, and was clearly on the point of saying something further, when he changed his mind and frowned thoughtfully at the ceiling for some while. Mr. Tridge, with arms doggedly folded, stared at him in resolute opposition.

“As a matter of fact, Joe,” said Mr. Dobb, at last, “you’re on quite the wrong tack. Prize-fighters ain’t got nothing to do with it.”

“Then what did you drag ’em in for?” countered Mr. Tridge.

“I only wanted to see if you knew what kind of chaps prize-fighters was like to get into trouble with.”

“Well, and what did you want to know that for?” queried Mr. Tridge, vigilantly.

“So as to see whether you’d realize, by comparison, what a very different sort of job this is I’m offering you.”

“’Ave it your own way,” said Mr. Tridge, guardedly. “You go on and say all you’ve got to say, and I’ll listen. That’s all I’ll promise.”

Thus encouraged, Mr. Dobb began to entertain his old shipmate with a character sketch of a certain Mr. Jevvings, Christian name either Haugustas or Hadolphus.

But whatever uncertainty Mr. Dobb might have as to Mr. Jevvings’ correct baptismal name, he had none as to Mr. Jevvings’ character. Mr. Jevvings, testified Horace, was a sport, a nut, a scorcher, a lad of the village, and a real caution. Also, it appeared, he was a knockout, a go-er, and, likewise, a cough-drop. Alternatively, he was also the limit. Mr. Tridge, nodding his head sapiently over these titles to fame, epitomized them all in the surmise that Mr. Jevvings must be a lively sort of card, and this description of the young gentleman gained Mr. Dobb’s cordial agreement.

Blessed with a gay disposition, an abundance of cash, and a widespread reputation for boisterous exploits, one might have expected that Mr. Jevvings found life replete with satisfaction. But, no! said Mr. Dobb. Oh, dear, no! There was something which inexorably qualified Mr. Jevvings’ enjoyment of existence. As Mr. Dobb phrased it, there was always a wasp in Mr. Jevvings’ jam.

It seemed that that young gentleman, although of average build, sadly lacked physical prowess, so much so that, in some of his roystering adventures, antagonists had thought nothing of playfully ruffling his hair prior to throwing him through a window. Courage in plenty had Mr. Jevvings, else would he long ago have retired into obscurity, but he had no skill at arms, and very frequently this precipitated an anticlimax in his spirited doings, so that they ended

unheroically for him. Too often, in fact, had this happened of late, and consequently Mr. Jevvings' reputation as a dashing blade was beginning to be clouded by a certain ribald contempt for his activities.

These things did Mr. Dobb explain to Mr. Tridge, in the terms most easily understanded of his old shipmate. Arrived at this point, he leaned impressively forward and tapped Mr. Tridge on the knee.

"And now," stated Mr. Dobb, "'e's got a idea for making people like 'im more serious. He's going to 'ave a fight with some one and knock 'im clean out."

"But from what you've been telling me," objected Mr. Tridge, "'e couldn't knock a fly off the wall."

Mr. Dobb, sitting erect, favoured his friend with a vast lingering wink. Then he continued his exposition.

It appeared that Mr. Jevvings was a close acquaintance of Mr. Dobb's. Recently he had come unostentatiously to Mr. Dobb and had confessed to him the bitterness that was vexing his soul. It was, in fact, Mr. Dobb who had suggested a semi-public demonstration of his fistic powers which should compel admiration and respect. With this proposition Mr. Jevvings had fallen in so enthusiastically that he had left all arrangements, financial and otherwise, to be consummated by Mr. Dobb.

"So that's where *you* comes in," explained Mr. Dobb.

"I see," said Mr. Tridge, acutely. "I says something to 'im, 'e knocks me down, and I get twenty quid for it?".

"Oh, not so helementary as that, Joe!" replied Mr. Dobb, pained at such lack of artistic imagination. "It's got to be worked up to, neat and natural. And there's got to be time for people to talk about it, before it comes off, as well as after. It'll be a swell thing, fought out reg'lar in a boxing-ring, with seconds and all."

“And when ’e’s knocked me about long enough,” supposed Mr. Tridge, “down I goes, and takes the count-out?”

Roughly, agreed Mr. Dobb, that was about the size of it. But the preliminaries, he pointed out, would need careful handling to create sufficient stir to satisfy Mr. Jevvings, and also Mr. Tridge would be required to take enough punishment to make the affair look convincing ere he succumbed to Mr. Jevvings’ knockout blow. This, he explained, was the voluntary humiliation and suffering to which he had alluded earlier in the evening.

“Well, if ’e’s ’alf the rabbit you make ’im out to be, ’e can’t ’urt me much,” complacently theorized Mr. Tridge; “and, as for ’umiliation, I’ve been ’umiliated for nothing at all in police-courts before now, so I certainly don’t mind being ’umiliated for money.”

Mr. Dobb, warmly eulogizing Mr. Tridge’s philosophy, assured him that the money was safe enough. Once arrangements were in trim for the combat, he—Mr. Dobb—would hold himself personally responsible for its payment.

“And we’ll set the ball rolling this very night,” said Mr. Dobb, with a computative glance at the clock. “Jevvings’ll be up in the ‘Rose and Crown,’ along of some of ’is pals. You must manage to get into a haltercation with ’im straightway, and leave the rest to me and one or two others what are in the know. We’ll see that a boxing match is fixed up between you, and you can leave all the arrangements to us.”

To all this Mr. Tridge assented with perfect readiness. Mr. Dobb then added a few simple instructions, and, after a single rehearsal, pronounced Mr. Tridge perfect in his role. Summoning his wife from some remote apartment, Mr. Dobb affably slipped his arm through Mr. Tridge’s, and the pair set off for the “Rose and Crown.”

“That’s ’im—that’s Jevvings!” whispered Horace, as they entered the crowded saloon bar. “That quiet-looking young feller in the check suit, with the pink tie, sitting reading the noospaper with patent leather boots on.”

Mr. Tridge, with a nod of comprehension, began to cross the floor. He was in the act of passing the young man when he stumbled clumsily, and, to preserve his balance, first knocked off the young man's hat and next ripped the newspaper from his grasp.

"Why can't you keep your great feet out of the way?" bellowed Mr. Tridge, furiously. "You ought to sit with 'em sticking out of the window, the size they are! You don't want patent leather on 'em—you wants red lamps on 'em and a watchman's box by the side of 'em! Of all the awkward—"

Mr. Jevvings, while preserving his calm under this onslaught, rose from his seat with a singularly sinister expression. Then, catching the expressive face of Mr. Dobb, he sat down again, a little helplessly. An awed hush had fallen on the room; frequenters of the apartment carefully setting down their glasses stared incredulously at the truculent Mr. Tridge.

"I must ask you to apologize!" said the aggrieved Mr. Jevvings, in a somewhat fluty voice.

"You ask away!" returned Mr. Tridge, with jocund ferocity. "You keep on till you're as black in the face as your blessed great boots! Apologize to a splay-footed whipper-snapper like you? Why, I'd sooner give you a smack in the eye! Far sooner! And so I would, too, for two pins!"

A sort of stifling surprise agitated the room and those gentlemen who were in the forefront of the quarrel cautiously stood back, while those on the outer rim of the altercation craned eagerly forward.

"If you don't apologize," said Mr. Jevvings, firmly, "I shall thrash you!"

"Ho, yus, *hin*-deed!" derided Mr. Tridge. "Come on, then!" he invited, and posed himself combatantly.

Audible was the rustle of amazement that coursed through the spectators. Mr. Jevvings, rising, began to turn back his coat-cuffs. There was a tense hush.

And then, as the folds of a curtain may come sweeping down to suspend the action of a play, so did Mr. Horace Dobb and the landlord of the “Rose and Crown” effectively intervene at this juncture.

With a deft certainty of grasp, Mr. Dobb and the landlord took command of affairs. Smoothly and swiftly did they regularize the situation. Building from the foundation that a mere rough-and-ready scrap was unthinkable in the chaste altitudes of the “Rose and Crown’s” saloon bar, a scaffolding of suggestions was run up with a celerity which suggested previous consultations, and presently, within this scaffolding, the outlines took shape of a pugilistic encounter of considerable ceremony, involving a ring, judge, seconds, and all the other paraphernalia of the craft.

Mr. Tridge, listening interestedly, heard the arrangements brought to a conclusion with the fixing of a date at that day week for the encounter. Mr. Jevvings having signified his entire willingness to accept the terms of the contest, Mr. Tridge gave his own acquiescence to the programme, adding rather gratuitously that, on the Sunday afternoon following the contest he would call round at the hospital with a bunch of grapes for Mr. Jevvings. Alternately he proposed to send a handsome wreath of white flowers.

“Right you are, then—that’s all settled!” said Mr. Dobb, exchanging a glance of relief with the landlord. “And now, Joe, I think we’d better leave ’ere. Hettiquette, you know, hettiquettte! ’E was ’ere first, and it’s ’is privilege to remain.”

He seemed in some anxiety to remove Mr. Tridge from the scene, and, taking him by the arm, drew him to the door. Here he led the way out into the street. Mr. Tridge, with a farewell remark to the effect that his opponent would be well advised to catch measles before the week was out, was about to follow Mr. Dobb, when a stout gentleman solemnly stepped forward to pat his shoulder with approval.

“I admire your pluck,” stated the stout gentleman.

“Huh!” exclaimed Mr. Tridge, glancing scornfully at Mr. Jevvings. “It don’t need much pluck!”

“But you know who he is, don’t you?” asked the other, wonderingly.

“Don’t know and don’t care!” was Mr. Tridge’s reckless reply. “I shall expect to learn ’oo ’e is at the inquest, any way.”

“You don’t know who he is?” gasped the stout gentleman, and then he patted Mr. Tridge’s shoulder again, but this time it was commiseratingly. “Why, that’s Ted Burch—*you* know, *the* Ted Burch! ‘Toff’ Burch, the Swindon Slogger!”

“What?” squealed Mr. Tridge. “A—a—a prize-fighter?”

“Middleweight champion of—”

“But—but I thought ’is name was Jevvings?”

“So it is, *pro tem.*,” returned his informant. “He’s stopping here *nem. con.*, doing a little quiet training for a match he’s got next month against Billy Traske, of Birmingham, and—”

Mr. Tridge did not await further instruction concerning Mr. Edward Burch. He had passed through the door with extreme celerity and was already cantering passionately in pursuit of Mr. Horace Dobb. Speedily catching up with his quarry, Mr. Tridge seized him and charged him with the blackest of treachery towards an unsuspecting friend. Mr. Dobb, but slightly stirred by the accusation, obliquely admitted its truth by regretting that Mr. Tridge should so soon have learnt the truth about Mr. Burch.

“But—but what did you want to play me a trick like that *for*?” roared Mr. Tridge.

“Why, because you’d never else ’ave dared to do what you did,” calmly replied Mr. Dobb. “You said yourself you’d ’ave nothing whatever to do with prize-fighters. That’s why I ’ad to take all the trouble to make up all that yarn I told you about Jevvings being a wild young chap of this town. Otherwise I’d never have brought you up to the scratch.”

“Well, you don’t suppose I’m going any further with it, do you?” demanded Mr. Tridge. “*No* fear!”

“Oh, but you can’t back out now, Joe!” argued Mr. Dobb. “It ’ud look so silly and cowardly if you backed out now.”

“I don’t care ’ow it *looks* if I back out! I know ’ow it will *feel* if I *don’t* back out, anyway! I can’t think what possessed you to play such a silly trick on me! Getting me to agree to stand up to a professional boxer under false pretences! Why, I’ve half a mind—”

Mr. Dobb, beseeching Mr. Tridge to maintain calm, now promised to impart the exact truth of the matter, prefacing his statement with a catalogue of grisly things which he said he hoped would happen to him if he diverged from complete veracity by as much as a hair-breadth.

He admitted that Mr. Burch, otherwise Mr. Jevvings, was a pugilist of some prominence with a deserved fame for neat and businesslike finishes to his bouts. It was, it transpired, the aim and ideal of Mr. Burch to put a similarly neat and businesslike finish to his forthcoming encounter with Mr. William Traske, of Birmingham. And, indeed, there was not the slightest doubt of Mr. Burch’s ability to do so. Unfortunately, there were others who held the same confidence as to the result, and this materially affected the betting on the issue of the match. In short, so overwhelmingly was Mr. Burch the favourite that it had become a matter of extreme difficulty to find anyone willing to bet against him, no matter how tempting the odds.

In these circumstances, it was thought expedient that something should transpire to lessen the popularity of Mr. Burch in betting circles. The landlord of the “Rose and Crown,” a party vested with considerable financial interests in Mr. Burch, had talked the matter over with other supporters, and together they had agreed on a plan. Further, the landlord of the “Rose and Crown,” being a close friend of Mr. Dobb’s and conversant with his abilities for organization, had called him in counsel and enlisted his services in the matter.

Briefly the scheme was this. Mr. Burch was to become involved in a quarrel with a local nobody, and to agree to settle the difference with boxing-gloves. Mr. Burch was to perform but indifferently at this match, failing to make the most of opportunities, and not getting in the knock-out blow till the twentieth round. There were spies in the Burch camp, and this strange remissness of his would indubitably be reported leading to a resurgence of confidence among the supporters of Mr. Traske, and so creating a profitable reaction on the betting market.

“But they’ll twig it’s a put-up job,” contended Mr. Tridge.

“No, they won’t, not them! You see, the affair’s supposed to be kept very quiet. Of course, it’s really a matter of hadvertisement, to hadvertise that Burch ’as gone dead off form; but seeing that it’s a personal matter ’e’s fighting about, they’ll never dream ’e ain’t in earnest.”

Here, then, concluded Mr. Dobb, was the real office that Mr. Tridge was required to fill, and the only difference in it to that which he had aforetime imagined it to be was that he was expected to stand up to a professional boxer of proved ability, instead of a mere amateur of indifferent skill.

“The fighting part’s just the same,” pointed out Mr. Dobb. “You’ve only got to let ’im play about with you for a bit, and the twenty quid is yours.”

“*Play about*?” echoed Mr. Tridge.

“That’s all, Joe,” said Mr. Dobb, reassuringly. “And you get twenty quid for it. It’s a big sum, but I know we can rely on you to keep your mouth shut. And ’ere’s the ‘Jolly Sailors’—let’s turn in and talk it over quietly.”

This they proceeded to do, though, as time progressed, they talked less and less quietly. Mr. Dobb, after drawing over and over again an agreeable mental picture wherein Mr. Tridge, for a few paltry taps on the nose, was rewarded with a hair-dressing business of his very

own, at length won the admission from his friend that it seemed worth it, after all.

“’Course it is,” affirmed Mr. Dobb. “You can take a bit of punishment, can’t you?”

“I can *take* it all right,” acquiesced Mr. Tridge. “The worst of it is that I always takes it faster than I gives it.”

“Besides, Joe, ’e won’t ’it you very ’ard,” wheedled Mr. Dobb. “You see ’e’s got to give the idea that ’e’s out of form. And it won’t be till the twentieth round that ’e knocks you out, so you’ll ’ave plenty of time to get used to the idea.”

“And I might go down of my own haccord in the nineteenth,” said Mr. Tridge, brightly. “Then ’e won’t ’ave a chance to put me properly to sleep.”

So that, when at length the law of the land compelled the “Jolly Sailors” to be churlish with its hospitality, Mr. Tridge had promised that no effort should be lacking on his part to crown the match with success, and he and his old shipmate parted on the best of terms.

Next morning, however, Mr. Tridge’s courage had suffered a relapse. Calling on Mr. Dobb at an early hour, he proclaimed his intention to abjure the match. In vain did Mr. Dobb fawn upon him with honeyed words; in vain did Mr. Dobb conjure up for him a splendid vision of a barber’s shop with “J. Tridge” in big letters over the door. Mr. Tridge was obdurate to mere verbal blandishments. It was only when Mr. Dobb, in desperation, offered to come with him and enter into pourparlers for early occupation of the little shop Mr. Tridge knew to be standing empty, that that unwilling gladiator again agreed to hold to the terms of his contract.

And even then he managed things with so adroit a reluctance that, before the day was over, Mr. Dobb, to clinch matters more effectually, was jockeyed into standing surety for the rent of the little shop, so that Mr. Tridge could enter into tenancy straightway.

For the next twenty-four hours Mr. Tridge was occupied with pails and brooms, getting his establishment into order, to the exclusion of all thoughts about the impending combat. That night, however, he

was too tired to sleep, and next morning he again sought out Mr. Dobb to place his resignation in his hands. But Mr. Dobb treated the crisis diplomatically by advancing him the wherewithal to purchase sundry implements of the hair-dressing profession. And, after that, Mr. Tridge could not but vow that he would cause no further concern of mind, and this promise he loyally kept.

None the less a marked moodiness of manner overcame him as the day of the encounter drew near, and often his deportment was that of a man doomed to early disintegration. To cheer him, Mr. Dobb contrived for him a secret meeting with Mr. Burch, who revealed himself as quite an amiable young gentleman, and promised Mr. Tridge that he should receive no real hurt until the final blow of the contest.

“And that,” interpolated Mr. Dobb, encouragingly, “you won’t be in your senses to feel, Joe, for more than a millionth part of a second, so you needn’t worry about that.”

And so we come to the day of the meeting, with Mr. Tridge, now visibly a prey to the direst forebodings, and with but a pathetic interest in his hairdressing shop, ready for immediate opening. For hours Mr. Tridge had gazed round the tiny place, sighing profoundly, as one who has achieved an aim too late in life, or else he had fondled the shining new implements reverently, as if already they were relics.

Mr. Dobb did his best to dissipate these mournful fears, reporting to Mr. Tridge that his financial share in the affair was abundantly secure, and that as soon after the conclusion of the contest as Mr. Tridge was able to think clearly, the landlord of the “Rose and Crown” was empowered to pay out to Mr. Tridge twenty pounds, less the amount already advanced by Mr. Dobb. And also Horace had endeavoured to stimulate Mr. Tridge’s interest in life by causing to be affixed to the wall of the place of meeting a huge poster which announced the imminent opening of the Magnolia Toilet Saloon (proprietor, J. Tridge), Bridge Street, Shorehaven. At six o’clock that evening Mr. Tridge was disturbed in a singularly vain effort to secure

a little refreshing slumber, and was called upon to receive Mr. Peter Lock. Mr. Lock, at the earnest request of his old shipmate, had consented to act as Mr. Tridge's second, and by way of inculcating the proper bright spirit in his principal with a little facetiousness, he now entered the apartment with slow, measured tread, and with extraordinary gravity of mien.

"Joseph Tridge," announced Mr. Lock, sepulchrally, "your hour is come!"

"Don't go making a mock of sacred things!" irritably requested Mr. Tridge. "It ain't funny—not at this minute."

"Joseph Tridge," droned on Mr. Lock, undeterred, in the same hollow tones, "have you made your will?"

"It so 'appens," snapped Mr. Tridge, "I 'ave! This very hafternoon! Thanks be I ain't left nothing to grinning i-i-enas!"

Mr. Lock, perceiving that Mr. Tridge's nerves were not yet keyed to appreciation of personal badinage, now endeavoured to rally him by narrating to him a number of droll anecdotes, all of which Mr. Tridge received in stony silence. Mr. Lock was still indefatigably endeavouring to cheer his principal when the stout and venerable Mr. Samuel Clark made his appearance.

Mr. Clark essayed no levity of conversation. On the contrary, he crossed in silence to Mr. Tridge and gravely clasped his hand. This done, he patted Mr. Tridge on the shoulder with deep sympathy, shook his hand again, and then sat down with a long, deep sigh.

"Cheerful, *you* are!" growled Mr. Tridge. "What do you think you've come to—a fooneral?"

"Oh, no; not yet—not yet, Joe!" Mr. Clark made haste to reply. "But I must say I 'ad a most hextryordinary dream about you to-day. Most hextryordinary! I dreamed you was killed in this 'ere fight. Funny thing I should dream that, wasn't it?"

"*Funny*?" fulminated Mr. Tridge.

“Anyway,” interposed Mr. Lock, “dreams always goes by contraries. It’ll be the other chap what’ll—”

“In my dream,” said Mr. Clark, “the other chap was so overcome by ’orror that ’e ’anged ’isself. So there you are—take your choice!”

For some moments Mr. Tridge sat apparently considering the selection. Then suddenly he rose and looked sadly in the mirror, and next he went slowly round the room, gazing at every article as though in tender farewell. Finally, shaking his head, he passed out of the apartment, and, followed by Mr. Clark and Mr. Lock, made his way to the “Rose and Crown.”

Here he found Mr. Dobb, who professed keen relief at sight of him, and forthwith conducted him to a dressing-room attached to the arena. Mr. Lock now offered to his principal much sage advice with regard to the coming contest; but Mr. Tridge was too occupied in his own mournful meditations to give useful heed.

“What—not dressed yet?” asked Horace, in surprise, entering the cubicle presently. “Why, you’ll be late! The ’all’s packed to overflowing, and there’s three chaps fell through the skylight already!”

As one in a dream Mr. Tridge began to disrobe and, later, to habit himself in the athletic garb Horace had procured for him.

“Now, come along!” ordered Horace, impatiently. “And for goodness’ sake, Joe, stop your knees from rattling so loud, else the referee won’t be able to ’ear ’isself speak! And do try to look ’appier!”

“I can’t!” confessed Mr. Tridge.

And now events marched through a haze to meet Mr. Tridge. He was aware of being pushed on to a platform by Mr. Lock’s shoulder, of being introduced to a crowded audience, of being fitted with enormous gloves. He heard plaudits greet his name, and would automatically have smiled his acknowledgments had he had the least control over his features. He saw the graceful, well-knit, frame

of his adversary vividly super-imposed, as it were, on a cloud made up of seconds and attendants.

“Time!” declared an authoritative voice. Mr. Clark breathed on Mr. Tridge a final cheery but unteetotal wish for his good luck; Mr. Lock gave him a shove; and he found himself facing his opponent. He caught a glimpse of the Magnolia Shaving Saloon advertisement, and he subconsciously wondered whether a ceremonial black shutter had been included among the stock and fixtures.

Mr. Jevvings bore down on him, glove outstretched, for the etiquette of handshaking. As hand met hand, Mr. Jevvings winked surreptitiously at Mr. Tridge in token of remembrance of the terms of the secret treaty. A sudden alertness illumined Mr. Tridge’s mind.

And as Mr. Jevvings carelessly stepped back from the handshake, Mr. Tridge’s left arm shot out, unexpectedly and violently and accurately. With a terrific impact it landed squarely on the jaw of the unprepared Mr. Jevvings.

Mr. Jevvings momentarily had the illusion of sailing skyward. Then he landed on the floor with a resounding thud.

Mr. Tridge, palpitating almost tearfully ’twixt fear and hope, hovered near him; but he lay there inert, and they counted him out. And so Shorehaven’s most sensational boxing-bout came to an abrupt end at its very start.

Again high emotion wrapped a mist around Mr. Tridge, but now it was tinged with a roseate hue, for, lo! the fight was over and he was still alive, and, more wonderful still, uninjured. This alone he could apprehend with the forefront of his mind, but remoter regions of his brain took heed that there was cheering and drinking and speeches; there was abject worship from the stout Mr. Clark, warm commendation from Mr. Peter Lock. And, most gratifying of all, there was public presentation of the residue of the twenty pounds, correct to a penny, and also there was a collection which a dazed but approving audience supported to the extent of eleven pounds four and six.

Within an hour Mr. Tridge was being lionized in the bar-parlour. Men strove for the honour of buying drinks for him, feeling well repaid if he recognized their existence in return. Quite plutocratic people vied with each other for the privilege of speaking deferentially to him, and importantly bade each other hush when he condescended to voice his opinions on any subject. For Mr. Tridge had won a battle in record time against the wildest expectation, and was now a hero and had raised himself into the ranks of the Temporary Immortals.

Mr. Dobb alone appeared out of sympathy with the popular mood for acclamation. For some while he sat silently watching Mr. Tridge among his courtiers. At last, unable to repress his emotions any longer, he rose and led Mr. Tridge into the obscurity of the passage outside.

“What the dooce did you do it for?” irascibly demanded Horace.

“It was a hinspiration,” said Mr. Tridge, modestly. “Just as the start was called, I looked up and I see that hadvertisement of my saloon. Somehow it come into my ’ead all in a flash what you said about the match being all a matter of hadvertisement, and a idea come to me that almost blinded me. I didn’t see why I shouldn’t get the hadvertisement for me and my saloon. I could see ’ow everybody ’ud troop up to be shaved by a chap what ’ad knocked out Toff Burch of Swindon. I could see ’ow useful my reppytation would be to keep customers in order when they complained if I cut ’em. And then I done it. Almost before I could think ’ow I was to do it, I done it. I knew I shouldn’t get a better chance, I knew ’e wouldn’t be troubling at all and that ’e wasn’t hexpecting me to do anything, and I done it. And it come off.”

“’E’ll ’alf kill you for it later on,” prophesied Mr. Dobb, with malevolent satisfaction.

“Oh, no, ’e won’t! I’ve ’ad a chat with ’im since ’e come round. ’E was pretty sore about it, ’e owned, but ’e don’t so much mind now. For why? Already they’re hoffering three to one against ’im for ’is match with Traske of Birmingham. So ’e’s quite satisfied, after all. And I’ve took care to see that I ain’t hexpected to meet ’im again,

because I've been telling every one I'd made a vow long ago to give up boxing for hever from this night forth, and they all agrees with me that I couldn't 'ave made a better end-up."

"Well, every one else may be satisfied, but *I* ain't," said Mr. Dobb, a little awkwardly. "I'll tell you for why. Knowing 'ow things was planned I'd been making a good lot of bets at long odds on this match—fourteen pounds in all—against you, of course. And, seeing as you've upset everything, I reckon it 'ud only be friendly and fair, out of your collection and so forth, to make good a bit of my loss to me."

"Come round to-morrow when I open," invited Mr. Tridge, happily, "and you shall be the first customer and I'll shave you free. There!"

"Don't try to get out of it like that, Joe. Fair's fair! If you'd done what you was hexpected to I'd 'ave made money. As it is, I've lost it. And you've got your collection, and the rest of your twenty quid, and—"

"And I've got a motter, too, 'Orace," said Mr. Tridge, softly, turning to the door of the bar-parlour. "*It's the same as yours*," he ended, with a grin, as he returned to adulation.

EPISODE VI
“ALL’S FAIR—”

The single, succinct phrase, “Doings!” linked to an address and an hour, had been passed round among the former shipmates of that obsolete vessel the “Jane Gladys,” and this slogan, acting much after the manner of a Fiery Cross, had immediately rallied the old confederacy to a ready eagerness to stand shoulder to shoulder again to take toll of the world by the exercise of those devious methods at which they were so expert.

And now here, in the cosy back parlour of the little shop in Fore Street, was assembled that quartet upon whom long companionship in the “Jane Gladys” had conferred a sinister brotherhood in ignoble aims and disreputable ambitions; and though each member had passed into a divergent class of shore-abiding life, it was plain that they were all still closely united by a common passion for petty intrigue.

Informal presidency over the meeting was exercised by Mr. Horace Dobb. At Mr. Dobb’s right hand sat the trim and debonair Mr. Peter Lock. On Mr. Dobb’s left was the corpulent and venerable Mr. Samuel Clark, who, by virtue of his appointment of ferryman across the mouth of Shorehaven Harbour, still preserved some remnant of his former nautical environment. Opposite to Mr. Dobb was Mr. Joseph Tridge, who had fortuitously laid aside his maritime jersey to wear a cotton overall in that hairdressing shop which Fate and force had secured for him.

Despite the stimulating and still undisclosed purpose for which the assemblage had been convened, the opening stages of the reunion were largely made up of spaces of vaunting autobiography, contributed by each of the members in a jostling, ill-disciplined way, sometimes separately, but usually in a pressing, conflicting chorus.

Thus Mr. Clark recounted, with great glee, as an example of his acumen, an anecdote concerning a foreign client who was unfamiliar both with the British system of coinage and the current rate of payment for passage on a ferry-boat. Mr. Tridge, in a similar boastful spirit, rehearsed some of his most successful retorts to customers who complained of dull razors or blunt scissors or intrusive lather-brushes. Mr. Dobb, for his part, supplied glowing accounts of the profits to be derived from the second-hand business by a man who was neither unperceptive nor too scrupulously honest and Mr. Lock, not to be overshadowed, revealed many hitherto unsuspected ways by which a billiard-marker might add substantially to his income.

And so the time wore on very pleasantly, till at last Mr. Dobb, looking pointedly at the clock, cleared his throat, and leaning his folded arms on the table, patently assumed a waiting attitude. Instantly a hush intervened, and something of an electric thrill coursed through this old and tried combination of small adventurers, for the time for consideration of serious business was come.

“Well, ’ere we are,” said Mr. Dobb, gazing round on his fellows, “all well and truly hestablished in the town of Shore’aven, like we’ve always ’oped and planned. Sitting round bragging about our cleverness is all very well, but you know my motter, don’t you?”

“‘Strictly business!’” supplied Mr. Tridge. “And I only wish I ’ad ’alf the friendly pints together it must ’ave saved you!”

“It’s a good motter,” said Mr. Dobb, equably. “It’s saved me a lot of talk, anyway, when you chaps ’ave dropped round on the chance of borrering a bob or two. ‘Strictly business!’—that’s got to be the motter for all of us, from now on. We’ve only to work together, and we can make ourselves ’ated for twenty miles round Shore’aven.”

“We used to be ’ated for a ’undred miles round the poor old ‘Jane Gladys,’” recalled Mr. Tridge, regretfully.

“‘Strictly business!’—that’s got to be one of our motters,” continued Mr. Dobb. “And the other must be ‘’Elp one another!’”

“Well, I like that!” exploded Mr. Clark. “And only the day before yesterday you refused to let me ’ave a cracked old second-’and teapot on credit!”

“And now ’ere we are, all hassembled for a trial trip, so to speak,” said Mr. Dobb, blandly ignoring the interruption. “If we work it right, there’s a couple of quid in it for each of you.”

“And what do *you* take?” demanded Mr. Tridge.

“I take the risk,” answered Mr. Dobb, simply.

“Oh, well, what’s the hidea, anyway?” asked Mr. Lock. “The boss ’as only given me one night off from the saloon, so I can’t stop here till to-morrow while you and Joe gets arguing as to whether you’re a miser or a philanthro-what-is-it! I suppose you’ve got some notion to put before us? You generally have.”

“And I ’ave now.” Mr. Dobb assured him. “A good ’un, too! You know old George Pincott?”

“The chap what’s lately started in the second-hand business in opposition to you?” returned Mr. Lock. “Aye, I know him. He often drops in at our place for a game of billiards.”

“I know ’e does,” admitted Mr. Dobb. “I’ve been taking that into account.”

“I know ’im, too,” put in Mr. Tridge. “’E comes round to me every day for a shave.”

“So I understand,” said Mr. Dobb, dryly.

“’E’s doing pretty well for a new-comer, too, ain’t ’e?” queried Mr. Clark, not without suspicion of relish.

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